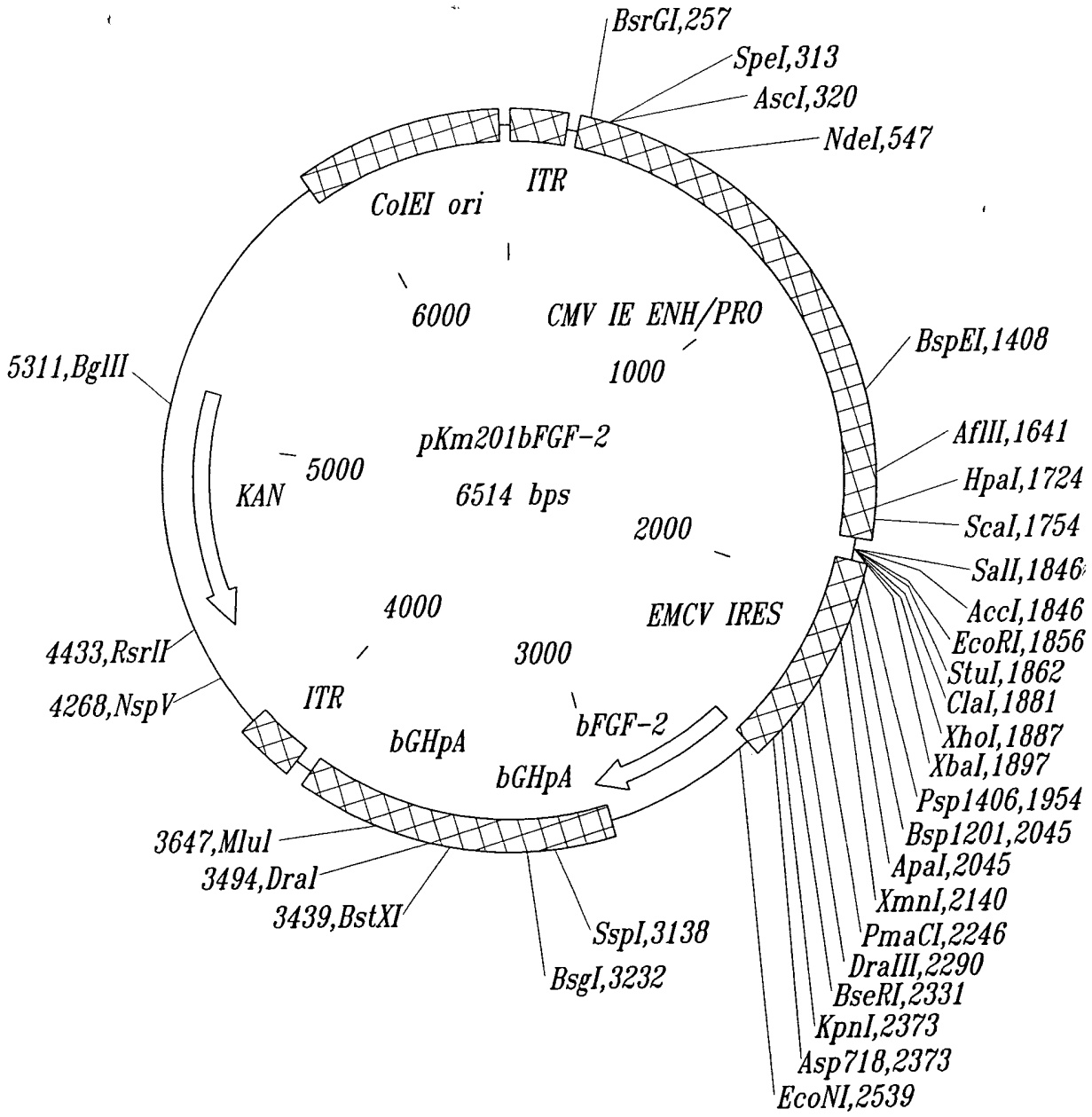
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SpeI,313
AscI,320
NdeI,547
ITR
ColEI ori
6000
CMV IE ENH/PRO
1000
BspEI,1408
5311,BglII
pKm201bFGF-2
6514 bps
AflII,1641
HpaI,1724
5000
KAN
ScaI,1754
2000
SalI,1846
AccI,1846
EcoRI,1856
StuI,1862
ClaI,1881
XhoI,1887
XbaI,1897
Psp1406,1954
Bsp1201,2045
ApaI,2045
XmnI,2140
PmaCI,2246
DraIII,2290
BseRI,2331
KpnI,2373
Asp718,2373
EcoNI,2539
4000
EMCV IRES
3000
4433,RsrII
4268,NspV
ITR
bGHpA
bFGF-2
bGHpA
3647,MluI
3494,DraI
3439,BstXI
SspI,3138
BsgI,3232

Fig. 1

ACCATGTAGCGGCCCTGCGCGCTCGCTCGCTCACTGAGGCCGCCCGGGCAAAGCCCGGGCGTCGGGCGACCTTTGGT
CGCCCGGCCTCAGTGAGCGAGCGAGCGCGCAGAGAGGGAGTGGCCAACTCCATCACTAGGGGTTCCTTGTAGTTAAT
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ATTGACTAGTTATTAATAGTAATCAATTACGGGGTCATTAGTTCATAGCCCATATATGGAGTTCCGCGTTACATAAC
TTACGGTAAATGGCCCGCCTGGCTGACCGCCCAACGACCCCCGCCCATTGACGTCAATAATGACGTATGTTCCCATA
GTAACGCCAATAGGGACTTTCCATTGACGTCAATGGGTGGAGTATTTACGGTAAACTGCCCACTTGGCAGTACATCA
AGTGTATCATATGCCAAGTCCGCCCCCTATTGACGTCAATGACGGTAAATGGCCCGCCTGGCATTATGCCCAGTACA
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Fig. 2A

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GATGCCTGTTGAATTATCGGATCCACTACGCGTTAGAGCTCGCTGATCAGCCTCGACTGTGCCTTCTAGTTGCCAGC
CATCTGTTGTTTGCCCCTCCCCCGTGCCTTCCTTGACCCTGGAAGGTGCCACTCCCACTGTCCTTTCCTAATAAAAT
GAGGAAATTGCATCGCATTGTCTGAGTAGGTGTCATTCTATTCTGGGGGGTGGGGTGGGGCAGGACAGCAAGGGGGA
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TCATCCAGCCGGCGTCCCGGAAAACGATTCCGAAGCCCAACCTTTCATAGAAGGCGGCGGTGGAATCGAAATCTCGT
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TCCTTTAGCAGCCCTTGCGCCCTGAGTGCTTGCGGCAGCGTGAAGCTGTCAATTCCGCGTTAAATTTTTGTTAAATC
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TGTTGTTCCAGTTTGGAACAAGAGTCCACTATTAAAGAACGTGGACTCCAACGTCAAAGGGCGAAAAACCGTCTATC
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AGAAGGACAGTATTTGGTATCTGCGCTCTGCTGAAGCCAGTTACCTTCGGAAAAAGAGTTGGTAGCTCTTGATCCGG
CAAACAAACCACCGCTGGTAGCGGCGGTTTTTTGTTTGCAAGCAGCAGATTACGCGCAGAAAAAAAGGATCTCAAGA
AGATCCTTTGATCTTTTCTTACTGAACGGTGATCCCCACCGGAATT

Fig. 2B

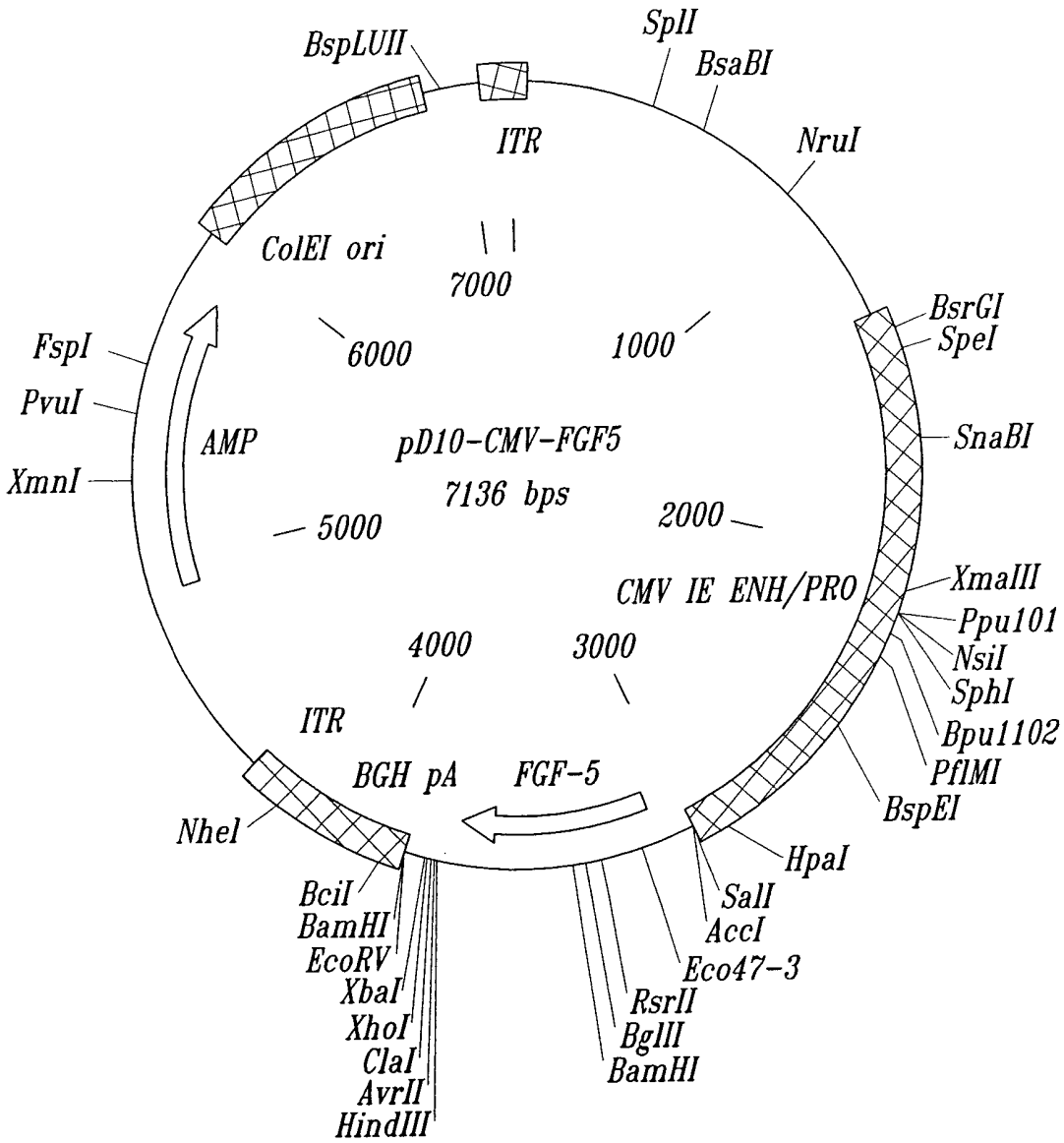

BspLUII
SpII
BsaBI
NruI
ITR
ColEI ori
7000
1000
6000
BsrGI
SpeI
FspI
PvuI
XmnI
AMP
pD10-CMV-FGF5
7136 bps
SnaBI
5000
2000
XmaIII
CMV IE ENH/PRO
Ppu101
4000
3000
NsiI
SphI
ITR
Bpu1102
PflMI
BGH pA
FGF-5
BspEI
NheI
HpaI
BciI
SalI
BamHI
AccI
EcoRV
Eco47-3
XbaI
RsrII
XhoI
BglII
ClaI
BamHI
AvrII
HindIII

Fig. 3

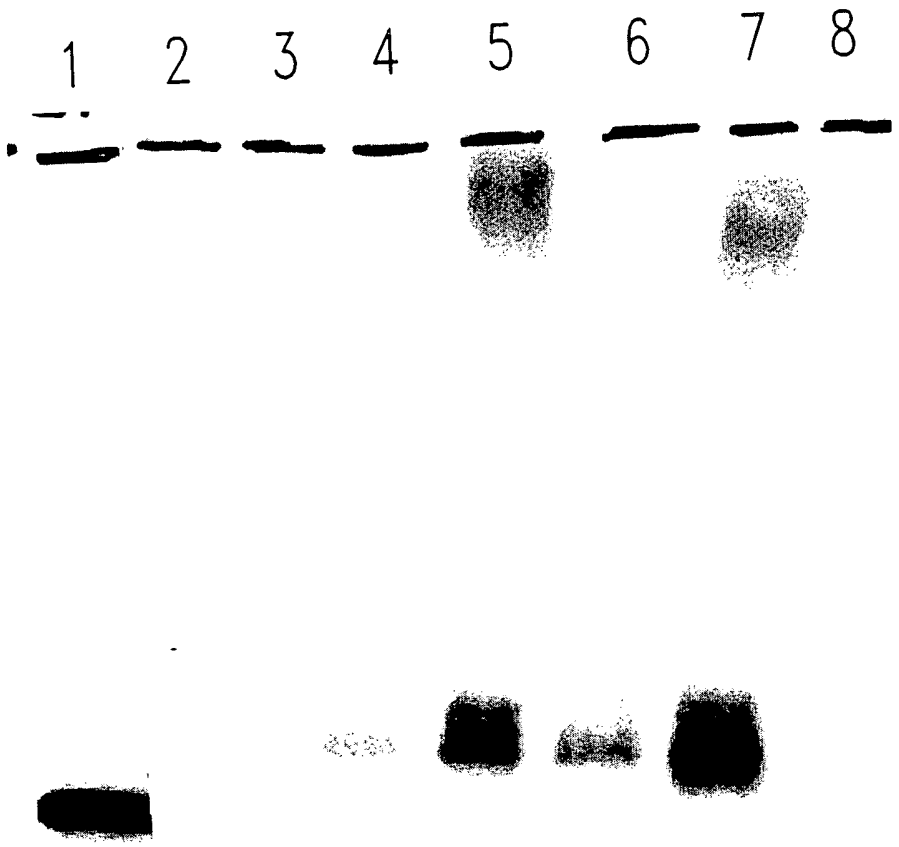
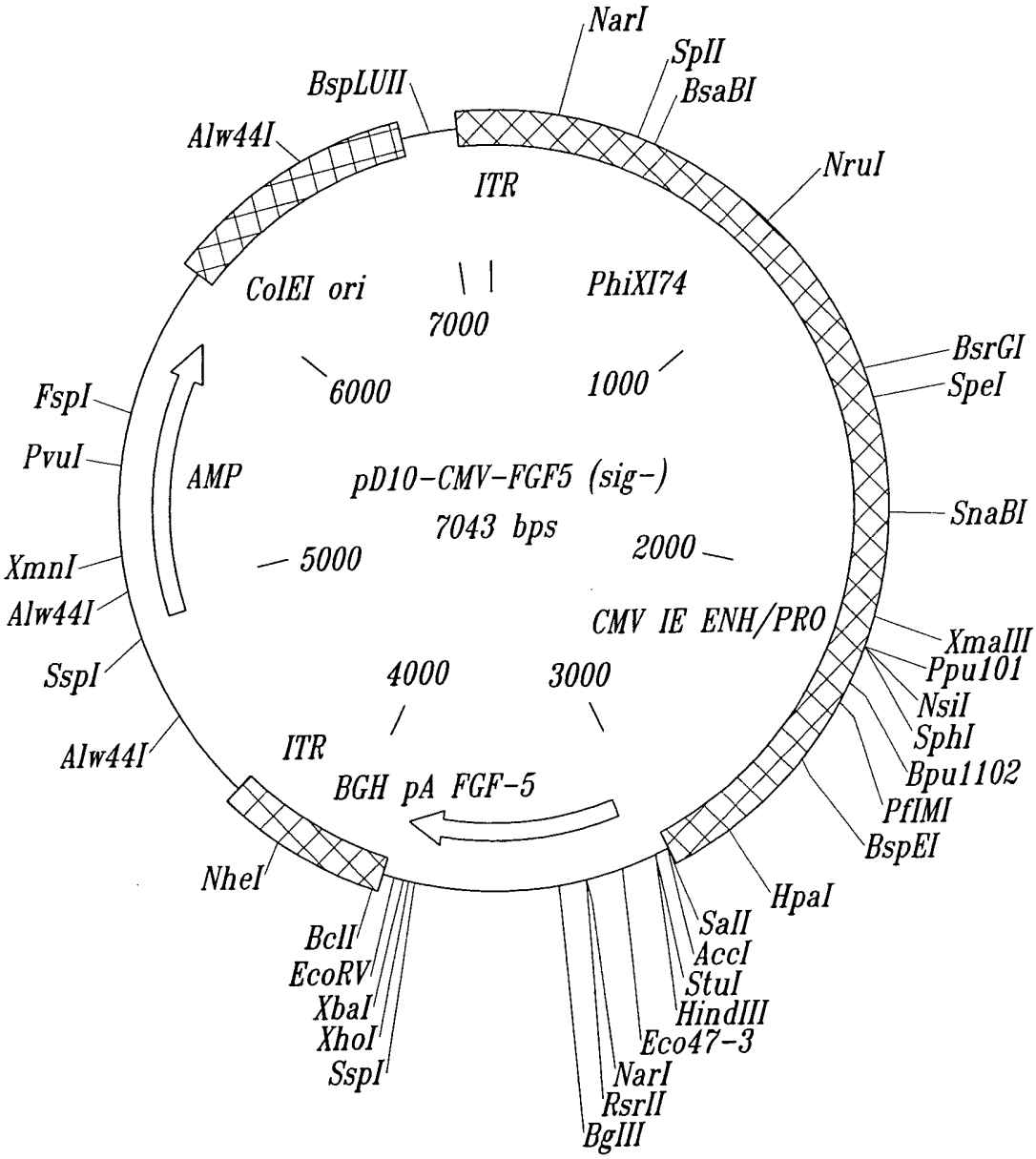


Fig. 4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SpII
BsaBI
BspLUII
Alw44I
NruI
ITR
ColEI ori
PhiXI74
7000
BsrGI
SpeI
FspI
6000
1000
PvuI
AMP
pD10-CMV-FGF5 (sig-)
SnaBI
7043 bps
XmnI
5000
2000
Alw44I
CMV IE ENH/PRO
XmaIII
Ppu101
SspI
4000
3000
NsiI
SphI
Alw44I
ITR
Bpu1102
BGH pA FGF-5
PflMI
BspEI
NheI
HpaI
SalI
BclI
AccI
EcoRV
StuI
XbaI
HindIII
XhoI
Eco47-3
SspI
NarI
RsrII
BglII

Fig. 5

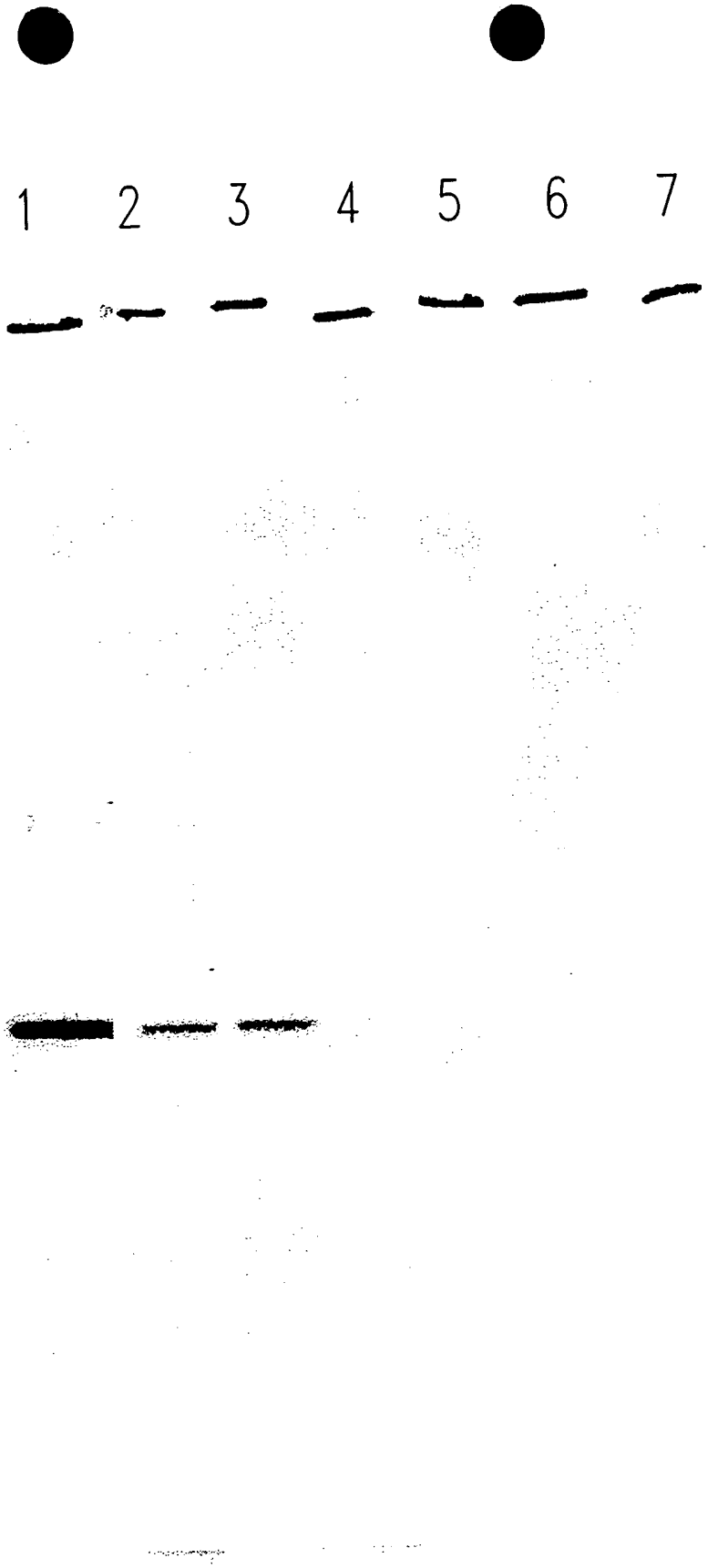
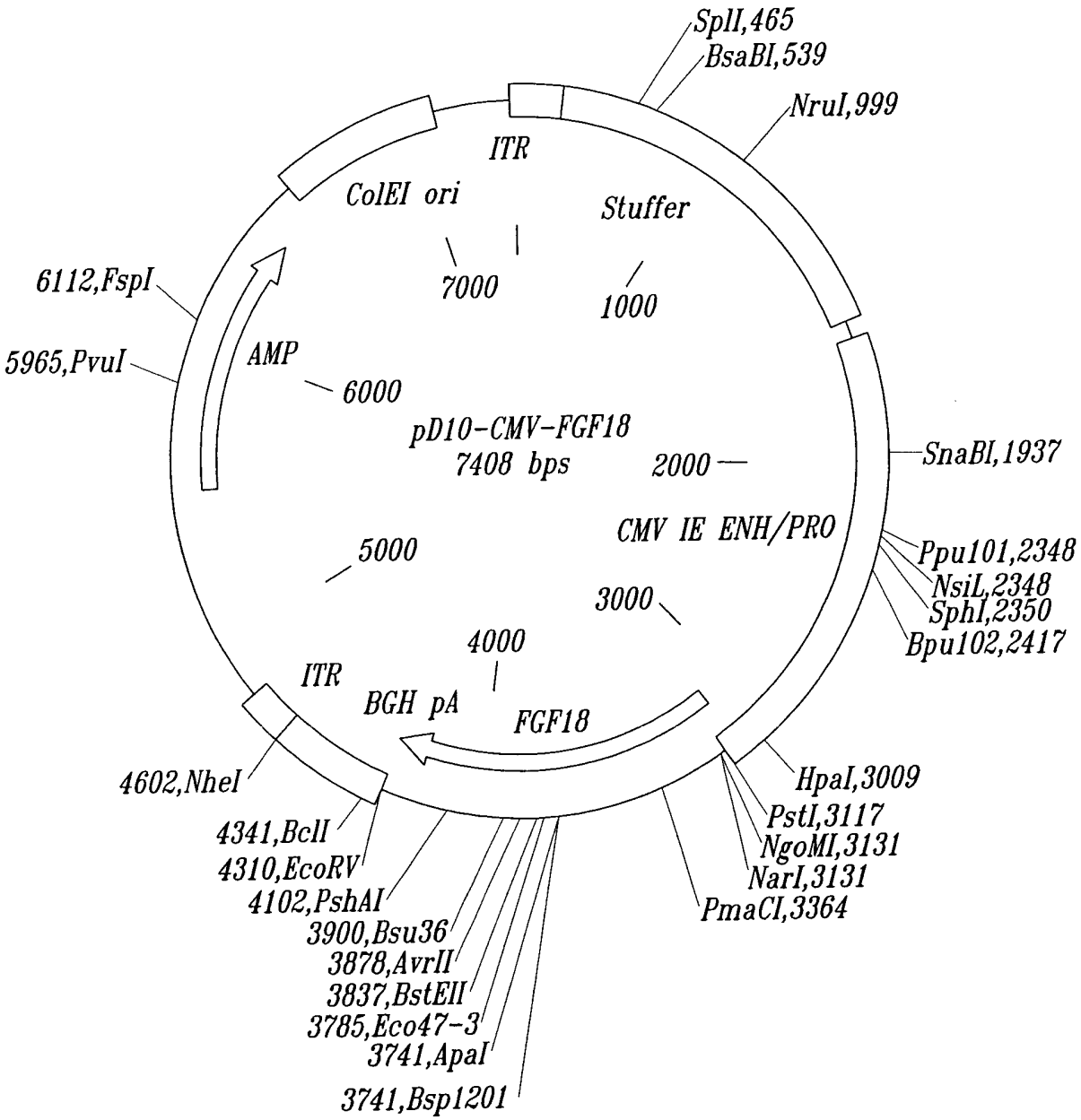


Fig. 6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BsaBI,539
NruI,999
ITR
ColEI ori
Stuffer
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1000
6112,FspI
5965,PvuI
AMP
6000
pD10-CMV-FGF18
7408 bps
2000
SnaBI,1937
CMV IE ENH/PRO
5000
Ppu101,2348
NsiL,2348
SphI,2350
Bpu102,2417
3000
4000
ITR
BGH pA
FGF18
HpaI,3009
PstI,3117
NgoMI,3131
NarI,3131
PmaCI,3364
4602,NheI
4341,BclI
4310,EcoRV
4102,PshAI
3900,Bsu36
3878,AvrII
3837,BstEII
3785,Eco47-3
3741,ApaI
3741,Bsp1201

Fig. 7

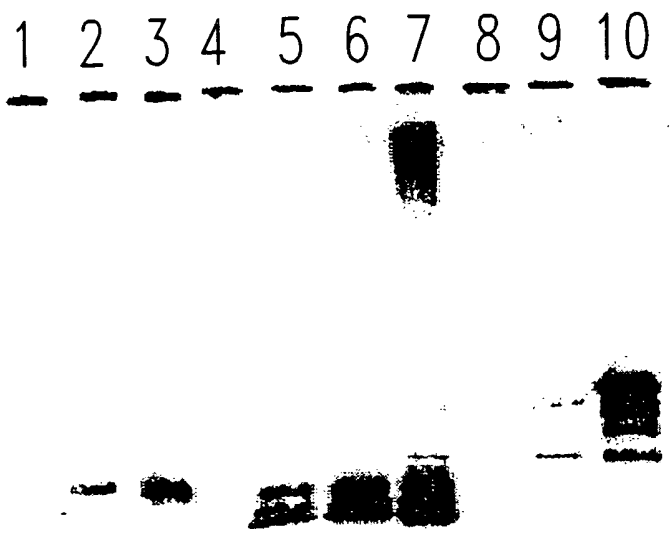


Fig. 8

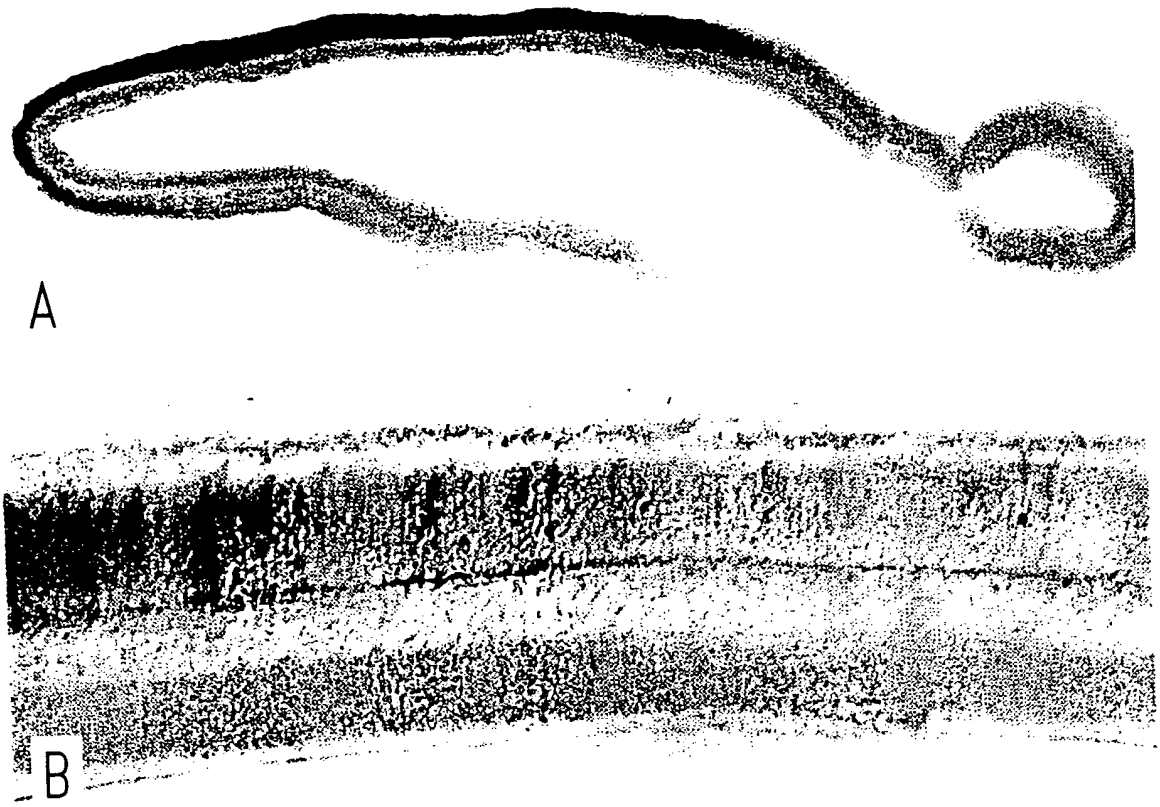


Fig. 9

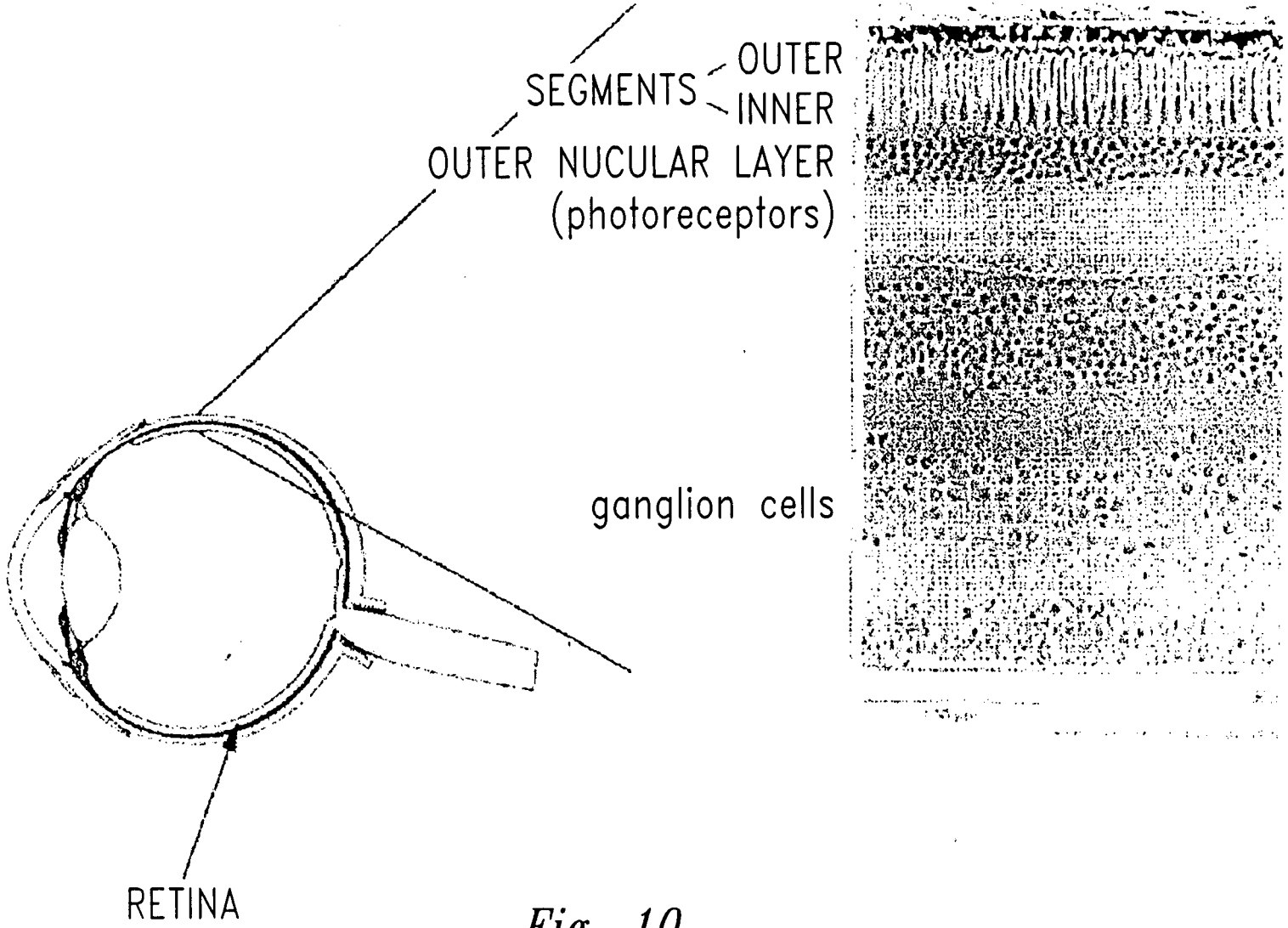

SEGMENTS
OUTER
INNER
OUTER NUCULAR LAYER
(photoreceptors)
ganglion cells
RETINA

Fig. 10

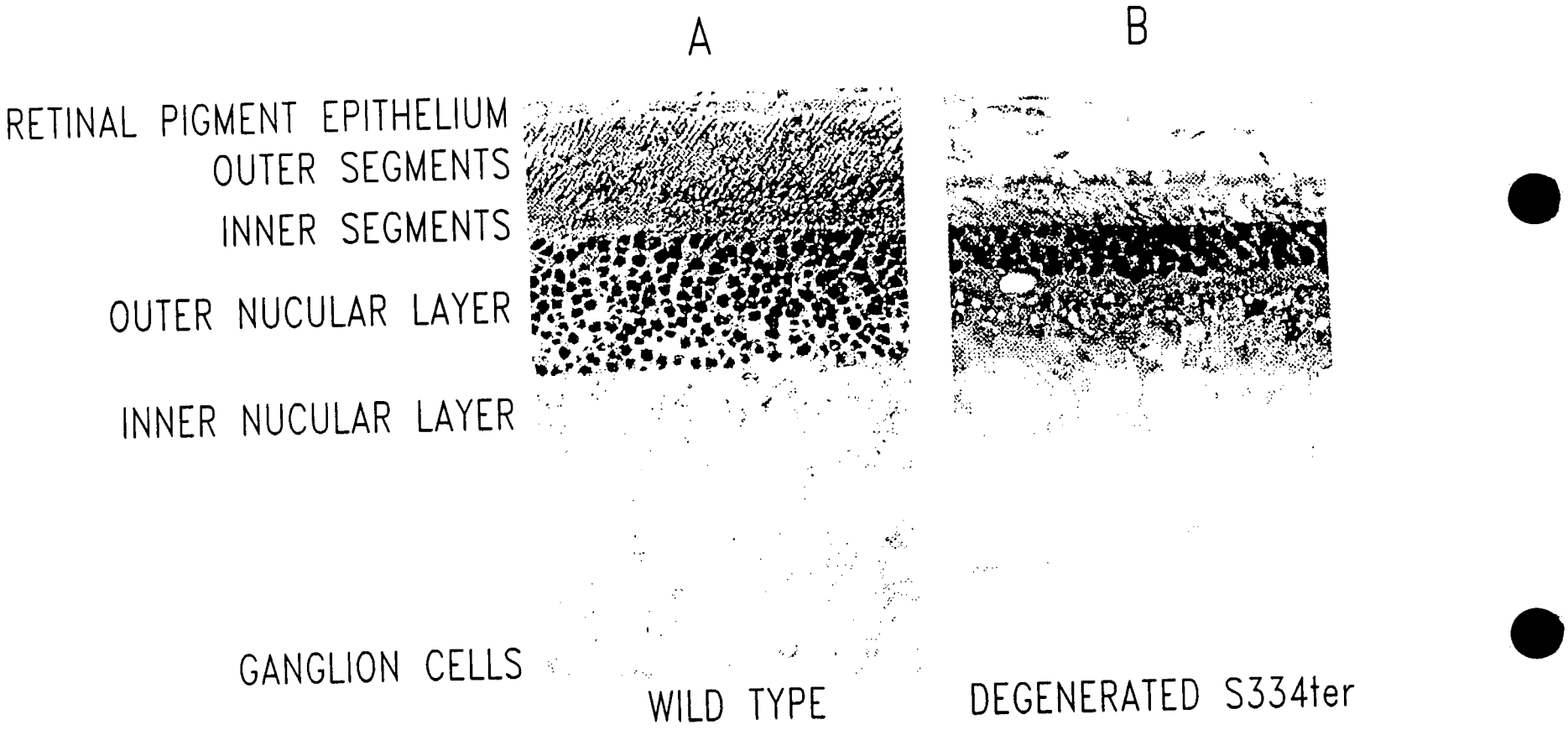


Fig. 11

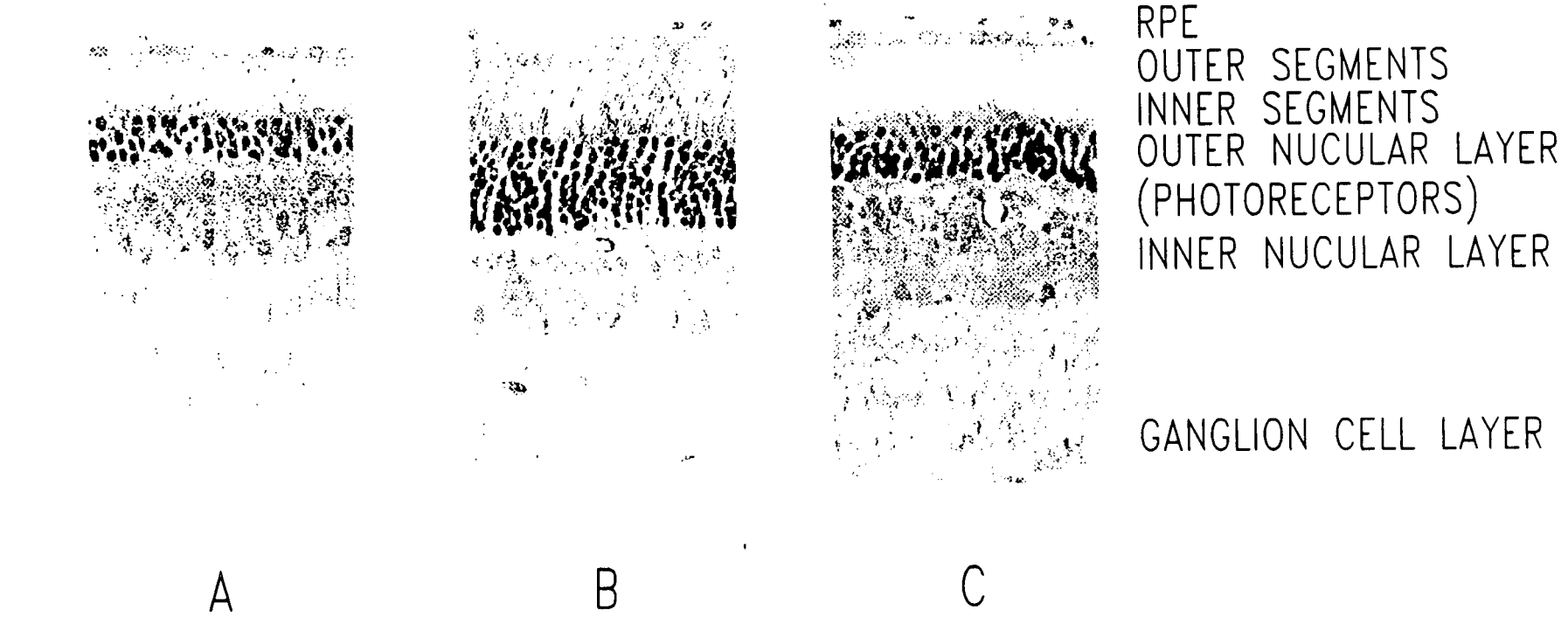

DEGENERATED S334ter
FGF-2 inj S334ter
PBS inj S334ter
RPE
OUTER SEGMENTS
INNER SEGMENTS
OUTER NUCULAR LAYER
(PHOTORECEPTORS)
INNER NUCULAR LAYER
GANGLION CELL LAYER
A
B
C

Fig. 12

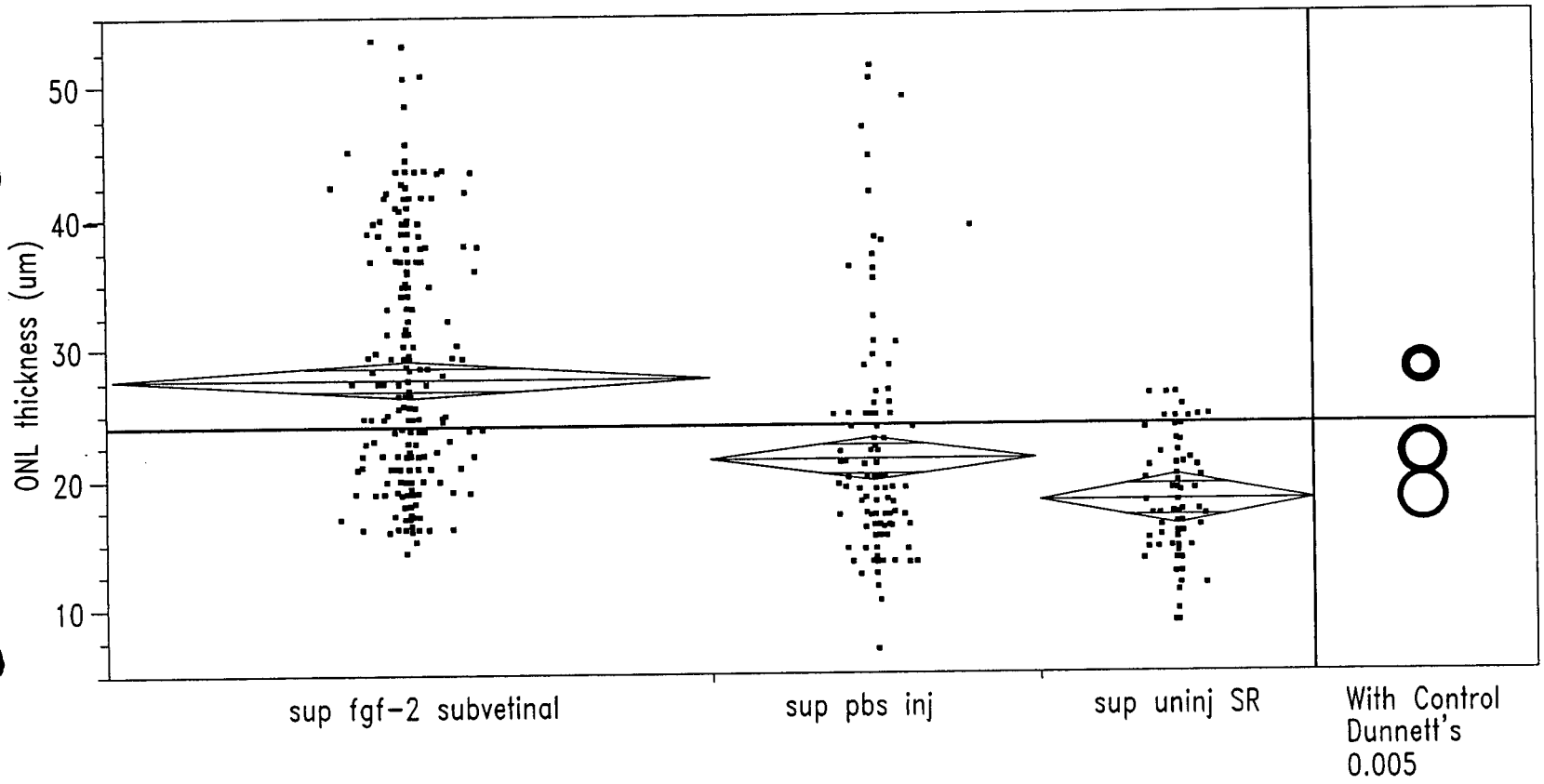


Fig. 13

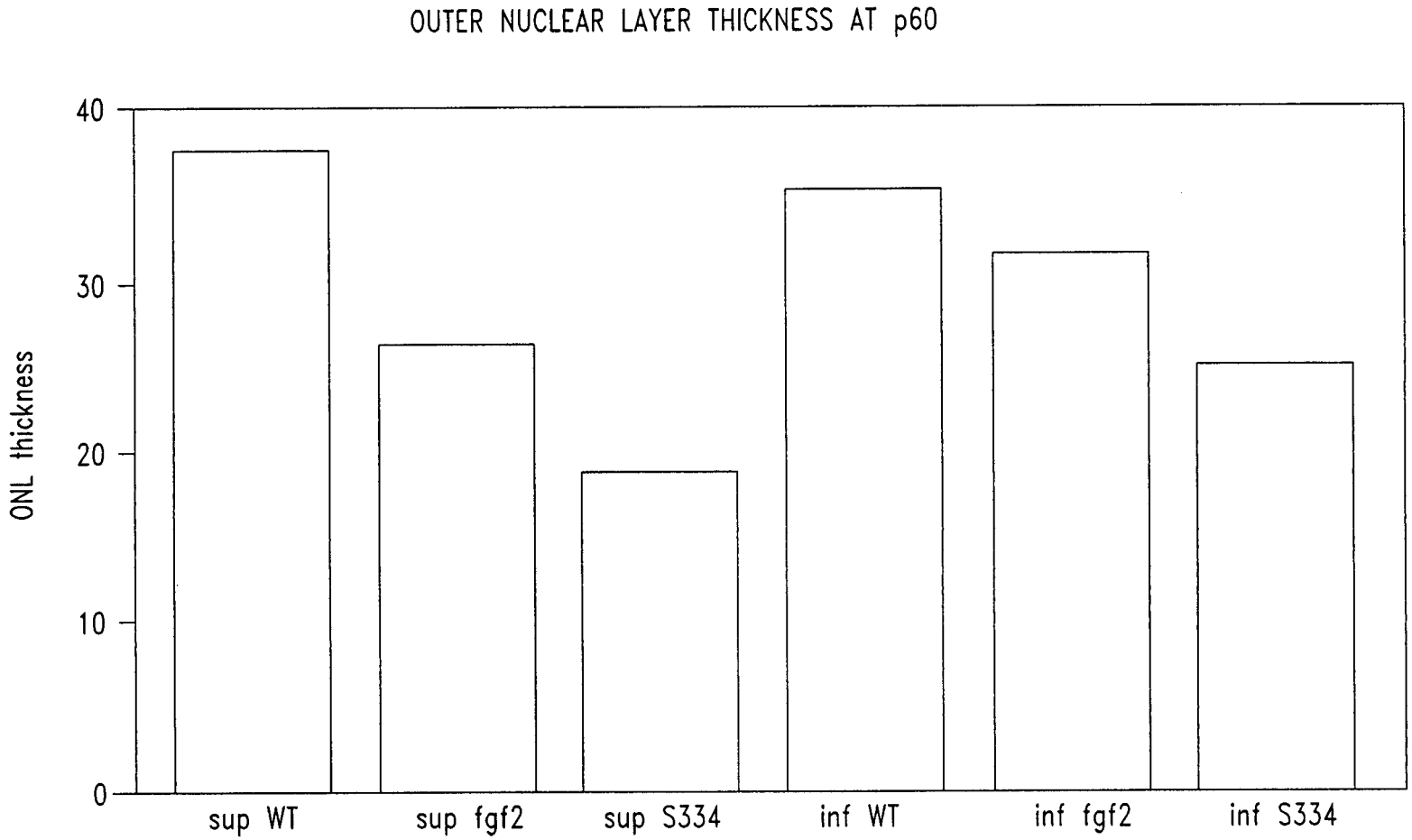

OUTER NUCLEAR LAYER THICKNESS AT p60
ONL thickness
40
30
20
10
0
sup WT
sup fgf2
sup S334
inf WT
inf fgf2
inf S334

Fig. 14

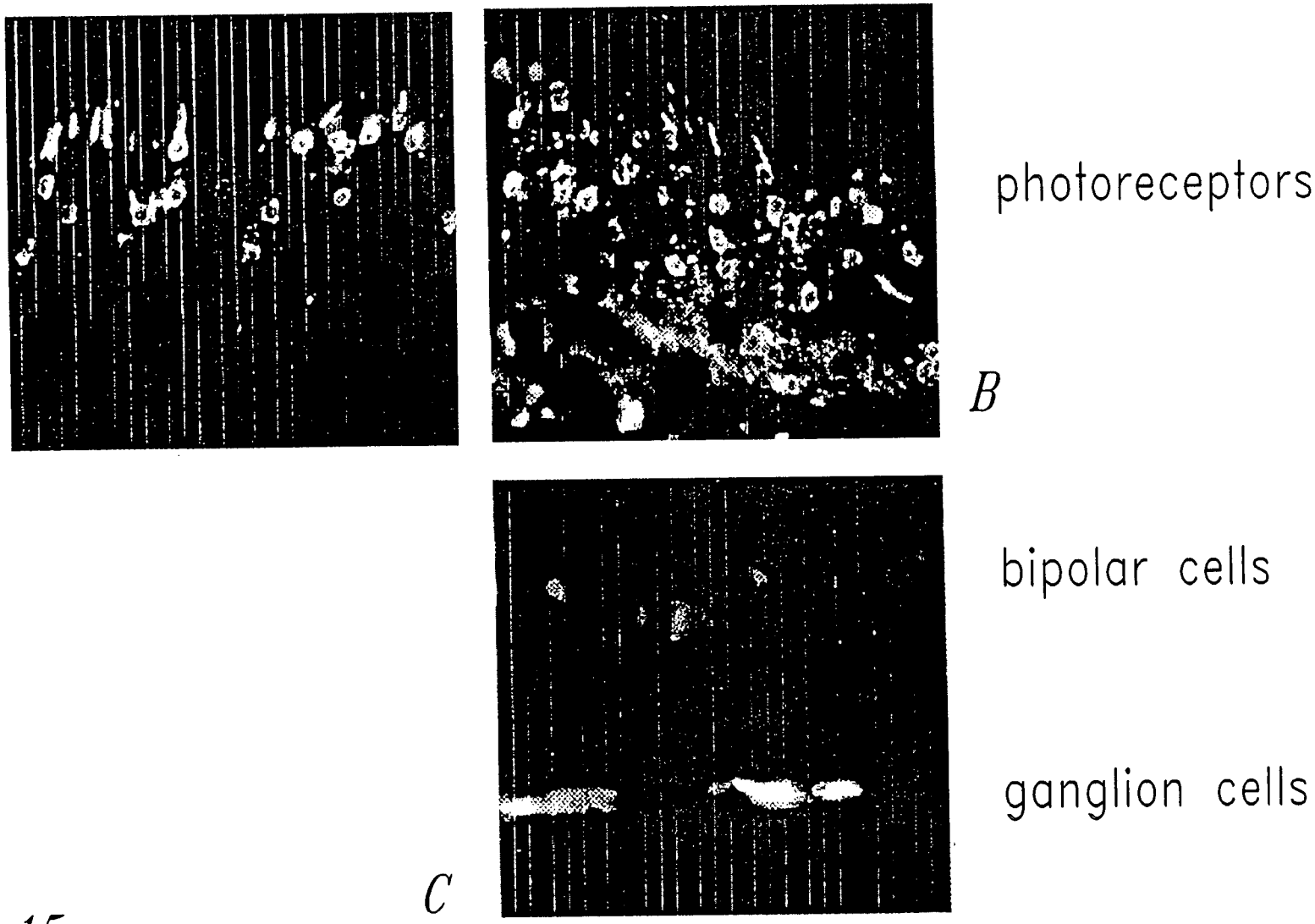


Fig. 15

AAV–LacZ Transduction of Retinal Ganglia

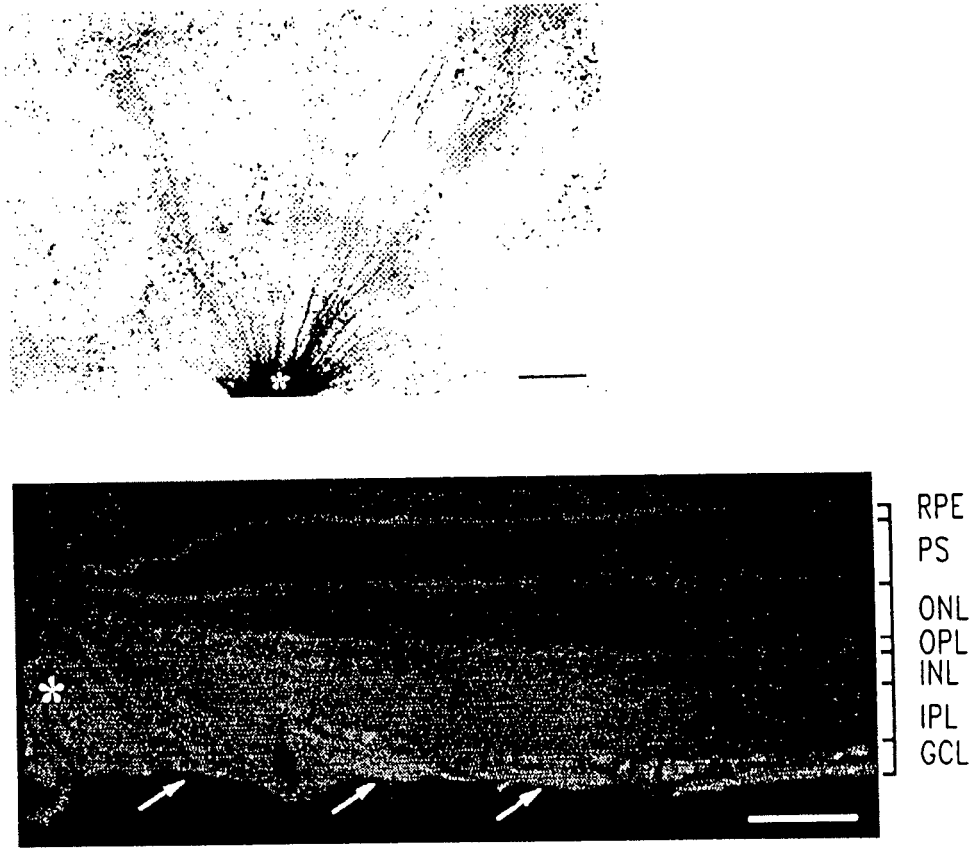


Fig. 16

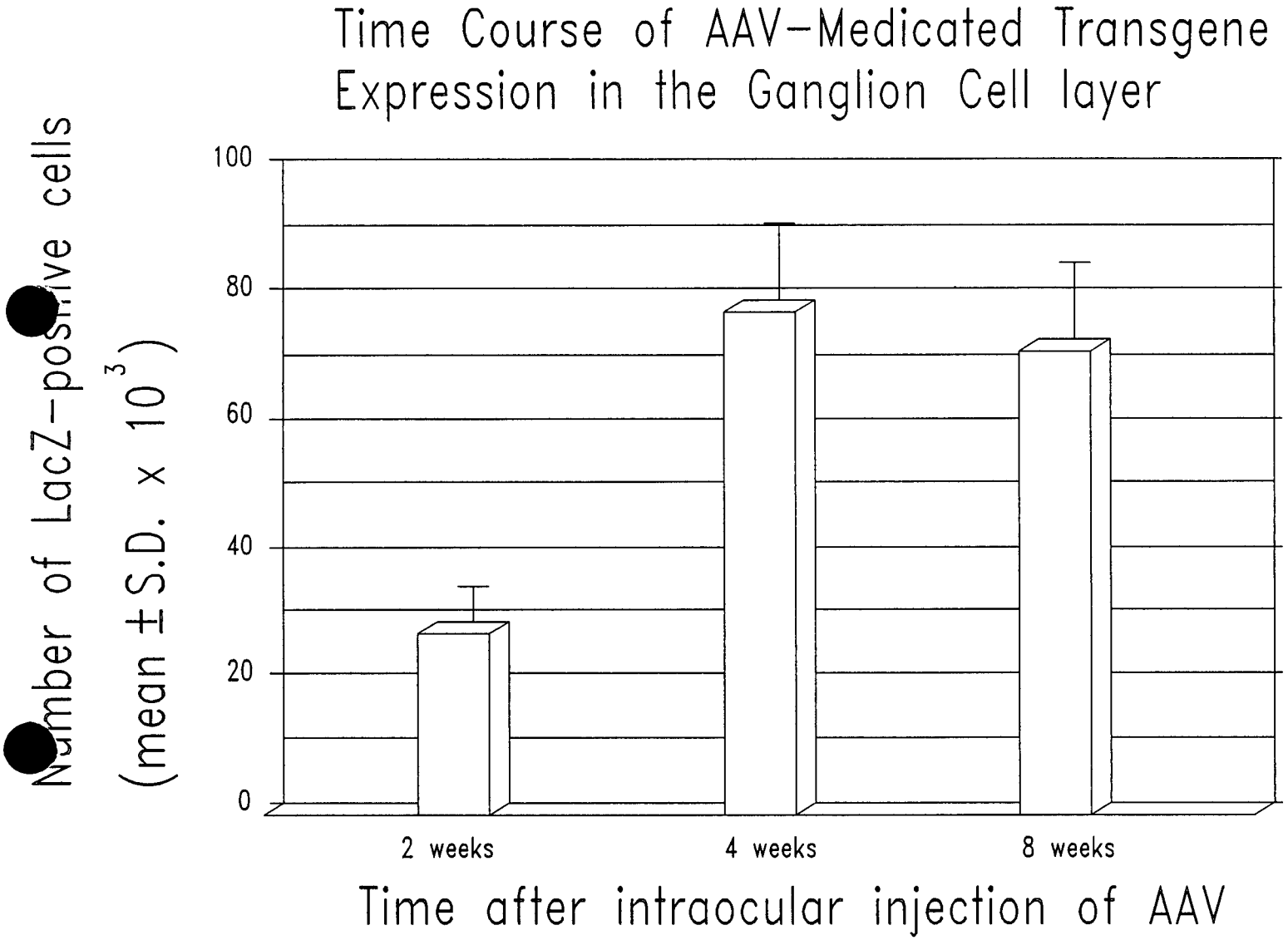
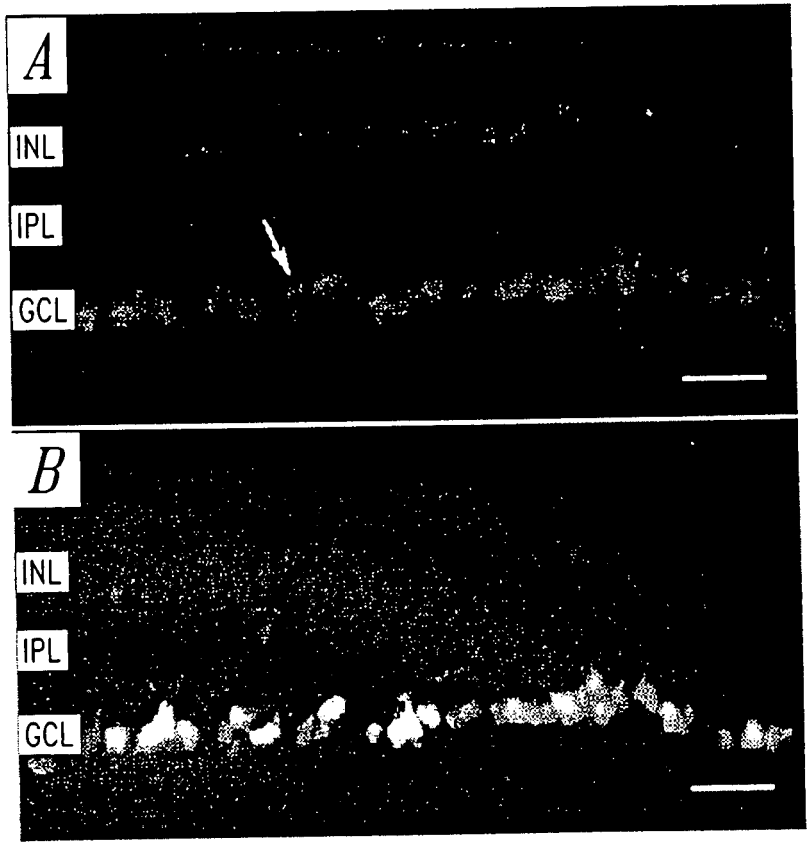

Time Course of AAV-Medicated Transgene Expression in the Ganglion Cell layer
Number of LacZ-positive cells
(mean ±S.D. x 10^3)
100
80
60
40
20
0
2 weeks
4 weeks
8 weeks
Time after intraocular injection of AAV

Fig. 17

Localization of AAV-Medicated LacZ Gene Product in Retrograde Labled RCG



α-LacZ

Fluorogold

Fig. 18

Quantification of Flourogold and LacZ Positive Cells in the Ganglion Cell Layer Following Intravitreal Injection of rAAV-LacZ

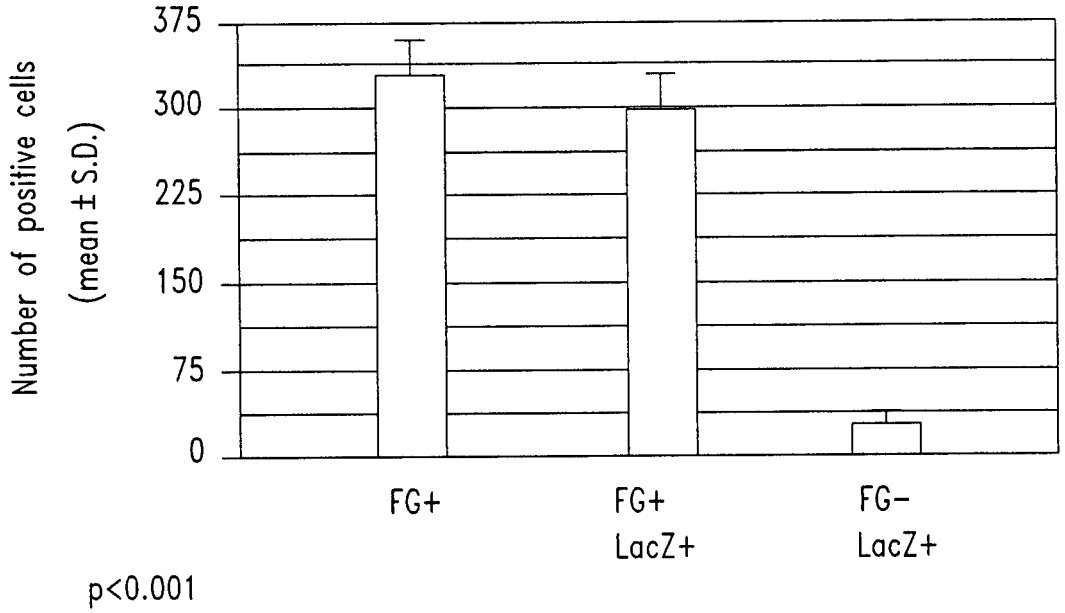


Fig. 19

Localization of Heparin sulfate Proteoglycan, the Cellular Receptor for AAV, in the Adult Rat Retina

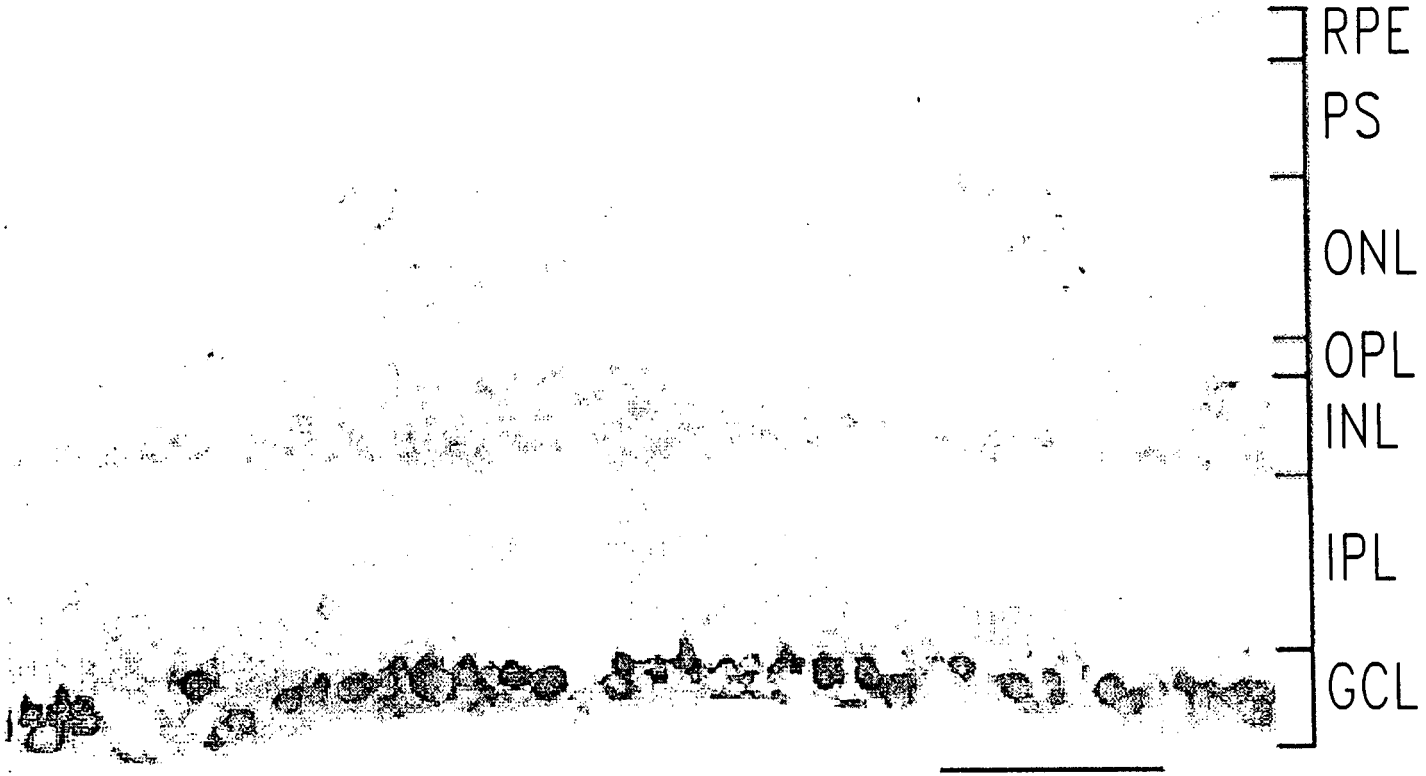
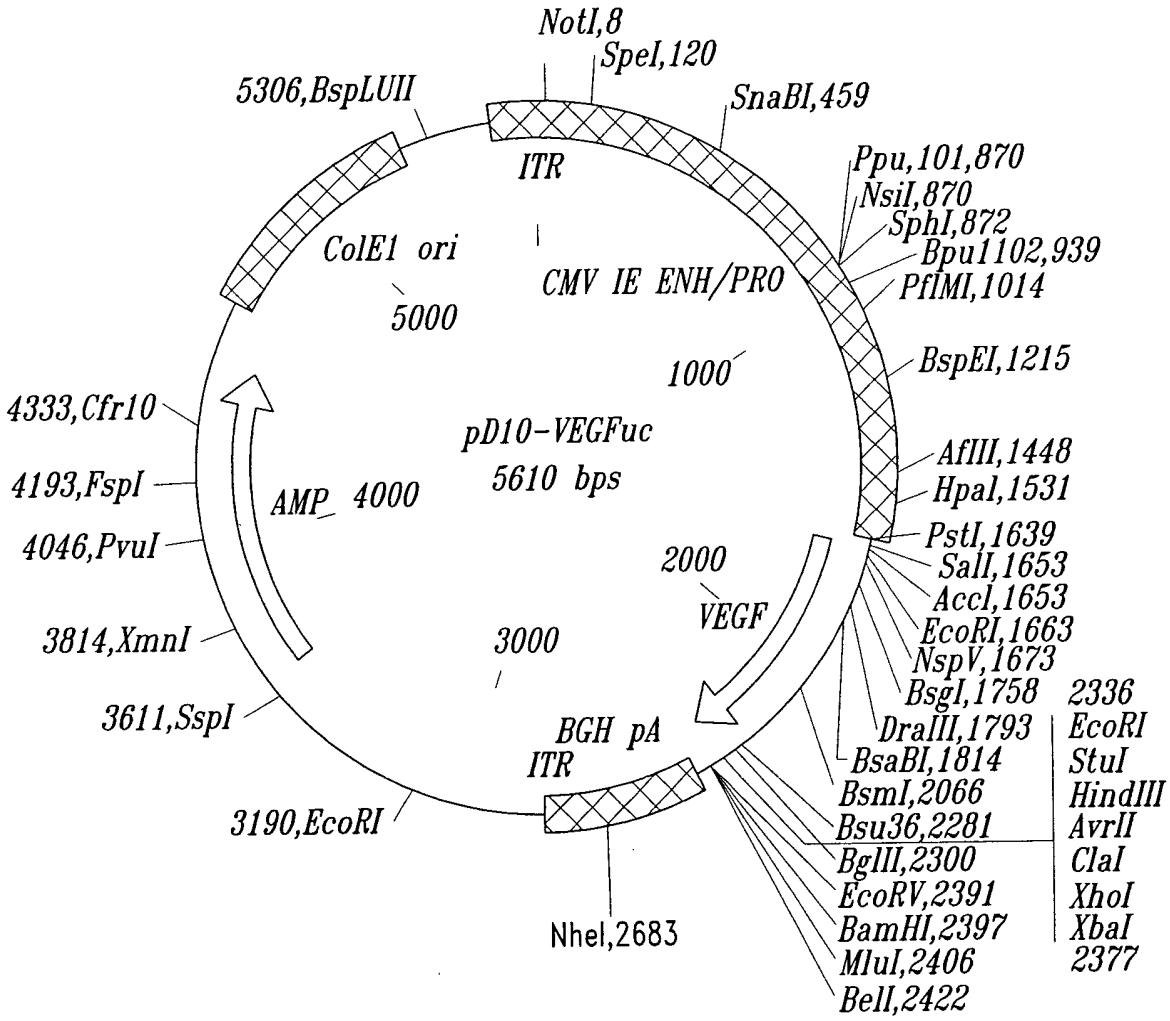


Fig. 20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SnaBI,459
5306,BspLUII
ITR
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NsiI,870
SphI,872
Bpu1102,939
PflMI,1014
ColE1 ori
5000
CMV IE ENH/PRO
1000
BspEI,1215
4333,Cfr10
pD10-VEGFuc
5610 bps
AfIII,1448
HpaI,1531
4193,FspI
AMP 4000
PstI,1639
SalI,1653
4046,PvuI
2000
AccI,1653
VEGF
EcoRI,1663
3814,XmnI
3000
NspV,1673
BsgI,1758
2336
3611,SspI
DraIII,1793
EcoRI
BGH pA
ITR
BsaBI,1814
StuI
3190,EcoRI
BsmI,2066
HindIII
Bsu36,2281
AvrII
BglII,2300
ClaI
EcoRV,2391
XhoI
NheI,2683
BamHI,2397
XbaI
MluI,2406
2377
BclI,2422

Fig. 21

Nucleotide Sequence of pD10-VEGFuc

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CCGTGCCAAGAGTGACGTAAGTACCGCCTATAGACTCTATAGGCACACCCCTTTGGCTCTTATGCATGCTATACTGTTTTTGGCTTGGGGCCTATACACCC
CCGCTCCTTATGCTATAGGTGATGGTATAGCTTAGCCTATAGGTGTGGGTTATTGACCATTATTGACCACTCCCCTATTGGTGACGATACTTTCCATTACT
AATCCATAACATGGCTCTTTGCCACAACTATCTCTATTGGCTATATGCCAATACTCTGTCCTTCAGAGACTGACACGGACTCTGTATTTTTACAGGATGGG
GTCCATTTATTATTTACAAATTCACATATACAACAACGCCGTCCCCCGTGCCCGCAGTTTTTATTAAACATAGCGTGGGATCTCCGACATCTCGGGTACGT
GTTCCGGACATGGGCTCTTCTCCGGTAGCGGCGGAGCTTCCACATCCGAGCCCTGGTCCCATCCGTCCAGCGGCTCATGGTCGCTCGGCAGCTCCTTGCTC
CTAACAGTGGAGGCCAGACTTAGGCACAGCACAATGCCCACCACCACCAGTGTGCCGCACAAGGCCGTGGCGGTAGGGTATGTGTCTGAAAATGAGCTCGG
AGATTGGGCTCGCACCTGGACGCAGATGGAAGACTTAAGGCAGCGGCAGAAGAAGATGCAGGCAGCTGAGTTGTTGTATTCTGATAAGAGTCAGAGGTAAC
TCCCGTTGCGGTGCTGTTAACGGTGGAGGGCAGTGTAGTCTGAGCAGTACTCGTTGCTGCCGCGCGCGCCACCAGACATAATAGCTGACAGACTAACAGAC
TGTTCCTTTCCATGGGTCTTTTCTGCAGTCACCGTCGTCGACCTAAGAATTCGCCCTTCGAAACCATGAACTTTCTGCTGTCTTGGGTGCATTGGAGCCTT
GCCTTGCTGCTCTACCTCCACCATGCCAAGTGGTCCCAGGCTGCACCCATGGCAGAAGGAGGAGGGCAGAATCATCACGAAGTGGTGAAGTTCATGGATGT
CTATCAGCGCAGCTACTGCCATCCAATCGAGACCCTGGTGGACATCTTCCAGGAGTACCCTGATGAGATCGAGTACATCTTCAAGCCATCCTGTGTGCCCC
TGATGCGATGCGGGGGCTGCTGCAATGACGAGGGCCTGGAGTGTGTGCCCACTGAGGAGTCCAACATCACCATGCAGATTATGCGGATCAAACCTCACCAA
GGCCAGCACATAGGAGAGATGAGCTTCCTACAGCACAACAAATGTGAATGCAGACCAAAGAAAGATAGAGCAAGACAAGAAAATCCCTGTGGGCCTTGCTC
AGAGCGGAGAAAGCATTTGTTTGTACAAGATCCGCAGACGTGTAAATGTTCCTGCAAAAACACAGACTCGCGTTGCAAGGCGAGGCAGCTTGAGTTAAACG
AACGTACTTGCAGATGTGACAAGCCGAGGCGGTGAGCCGGGCAGGAGGAAGGAGCCTCCCTCAGGGTTTCGGGAACCAGATCTCTCACCAGGAAAGACTGA
TACAGAAAGGGCGAATTCAGGCCTAAGCTTCCTAGGTATCGATCTCGAGCAAGTCTAGAAAGCCATGGATATCGGATCCACTACGCGTTAGAGCTCGCTGA
TCAGCCTCGACTGTGCCTTCTAGTTGCCAGCCATCTGTTGTTTGCCCCTCCCCCGTGCCTTCCTTGACCCTGGAAGGTGCCACTCCCACTGTCCTTTCCTA
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GCAGGGGGGTGGGCGAAGAACTCCAGCATGAGATCCCCGCGCTGGAGGATCATCCAGCTAGCAAGTCCCATCAGTGATGGAGTTGGCCACTCCCTCTCTGC
GCGCTCGCTCGCTCACTGAGGCCGGGCGACCAAAGGTCGCCCGACGCCCGGGCTTTGCCCGGGCGGCCTCAGTGAGCGAGCGAGCGCGCCAGCGATTCTCT
TGTTTGCTCCAGACTCTCAGGCAATGACCTGATAGCCTTTGTAGAGACCTCTCAAAAATAGCTACCCTCTCCGGCATGAATTTATCAGCTAGAACGGTTGA
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CTAAAAATTTTTATCCTTGCGTTGAAATAAAGGCTTCTCCCGCAAAAGTATTACAGGGTCATAATGTTTTTGGTACAACCGATTTAGCTTTATGCTCTGAG
GCTTTATTGCTTAATTTTGCTAATTCTTTGCCTTGCCTGTATGATTTATTGGATGTTGGAATTCCTGATGCGGTATTTTCTCCTTACGCATCTGTGCGGTA
TTTCACACCGCATATGGTGCACTCTCAGTACAATCTGCTCTGATGCCGCATAGTTAAGCCAGCCCCGACACCCGCCAACACCCGCTGACGCGCCCTGACGG
GCTTGTCTGCTCCCGGCATCCGCTTACAGACAAGCTGTGACCGTCTCCGGGAGCTGCATGTGTCAGAGGTTTTCACCGTCATCACCGAAACGCGCGAGACG
AAAGGGCCTCGTGATACGCCTATTTTTATAGGTTAATGTCATGATAATAATGGTTTCTTAGACGTCAGGTGGCACTTTTCGGGGAAATGTGCGCGGAACCC
CTATTTGTTTATTTTTCTAAATACATTCAAATATGTATCCGCTCATGAGACAATAACCCTGATAAATGCTTCAATAATATTGAAAAAGGAAGAGTATGAGT

Fig. 22A

ATTCAACATTTCCGTGTCGCCCTTATTCCCTTTTTTGCGGCATTTTGCCTTCCTGTTTTTGCTCACCCAGAAACGCTGGTGAAAGTAAAAGATGCTGAAGA
TCAGTTGGGTGCACGAGTGGGTTACATCGAACTGGATCTCAACAGCGGTAAGATCCTTGAGAGTTTTCGCCCCGAAGAACGTTTTCCAATGATGAGCACTT
TTAAAGTTCTGCTATGTGGCGCGGTATTATCCCGTATTGACGCCGGGCAAGAGCAACTCGGTCGCCGCATACACTATTCTCAGAATGACTTGGTTGAGTAC
TCACCAGTCACAGAAAAGCATCTTACGGATGGCATGACAGTAAGAGAATTATGCAGTGCTGCCATAACCATGAGTGATAACACTGCGGCCAACTTACTTCT
GACAACGATCGGAGGACCGAAGGAGCTAACCGCTTTTTTGCACAACATGGGGGATCATGTAACTCGCCTTGATCGTTGGGAACCGGAGCTGAATGAAGCCA
TACCAAACGACGAGCGTGACACCACGATGCCTGTAGCAATGGCAACAACGTTGCGCAAACTATTAACTGGCGAACTACTTACTCTAGCTTCCCGGCAACAA
TTAATAGACTGGATGGAGGCGGATAAAGTTGCAGGACCACTTCTGCGCTCGGCCCTTCCGGCTGGCTGGTTTATTGCTGATAAATCTGGAGCCGGTGAGCG
TGGGTCTCGCGGTATCATTGCAGCACTGGGGCCAGATGGTAAGCCCTCCCGTATCGTAGTTATCTACACGACGGGGAGTCAGGCAACTATGGATGAACGAA
ATAGACAGATCGCTGAGATAGGTGCCTCACTGATTAAGCATTGGTAACTGTCAGACCAAGTTTACTCATATATACTTTAGATTGATTTAAAACTTCATTTT
TAATTTAAAAGGATCTAGGTGAAGATCCTTTTTGATAATCTCATGACCAAAATCCCTTAACGTGAGTTTTCGTTCCACTGAGCGTCAGACCCCGTAGAAAA
GATCAAAGGATCTTCTTGAGATCCTTTTTTTCTGCGCGTAATCTGCTGCTTGCAAACAAAAAAACCACCGCTACCAGCGGTGGTTTGTTTGCCGGATCAAG
AGCTACCAACTCTTTTTCCGAAGGTAACTGGCTTCAGCAGAGCGCAGATACCAAATACTGTCCTTCTAGTGTAGCCGTAGTTAGGCCACCACTTCAAGAAC
TCTGTAGCACCGCCTACATACCTCGCTCTGCTAATCCTGTTACCAGTGGCTGCTGCCAGTGGCGATAAGTCGTGTCTTACCGGGTTGGACTCAAGACGATA
GTTACCGGATAAGGCGCAGCGGTCGGGCTGAACGGGGGGTTCGTGCACACAGCCCAGCTTGGAGCGAACGACCTACACCGAACTGAGATACCTACAGCGTG
AGCTATGAGAAAGCGCCACGCTTCCCGAAGGGAGAAAGGCGGACAGGTATCCGGTAAGCGGCAGGGTCGGAACAGGAGAGCGCACGAGGGAGCTTCCAGGG
GGAAACGCCTGGTATCTTTATAGTCCTGTCGGGTTTCGCCACCTCTGACTTGAGCGTCGATTTTTGTGATGCTCGTCAGGGGGGCGGAGCCTATGGAAAAA
CGCCAGCAACGCGGCCTTTTTACGGTTCCTGGCCTTTTGCTGGCCTTTTGCTCACATGTTCTTTCCTGCGTTATCCCCTGATTCTGTGGATAACCGTATTA
CCGCCTTTGAGTGAGCTGATACCGCTCGCCGCAGCCGAACGACCGAGCGCAGCGAGTCAGTGAGCGAGGAAGCGGAAGAGCGCCCAATACGCAAACCGCCT
CTCCCCGCGCGTTGGCCGATTCATTAATGCAGCTGGCGCGCTCGCTCGCTCACTGAGGCCGCCCGGGCAAAGCCCGGGCGTCGGGCGACCTTTGGTCGCCC
GGCCTCAGTGAGCGAGCGAGCGCGCAGAGAGGGAGTGGCCAACTCCATCACTGAT

Fig. 22B

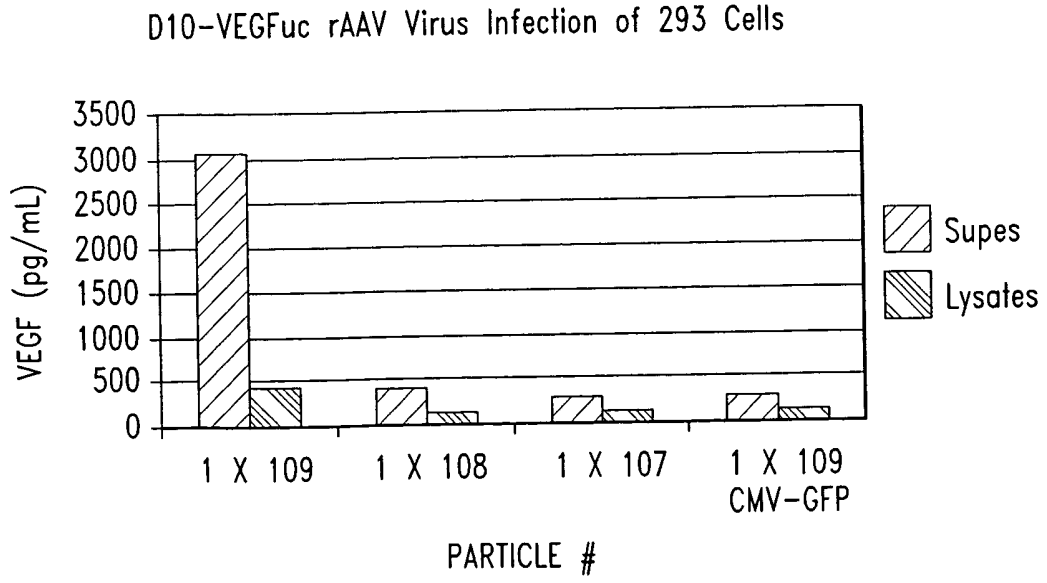

Fig. 23

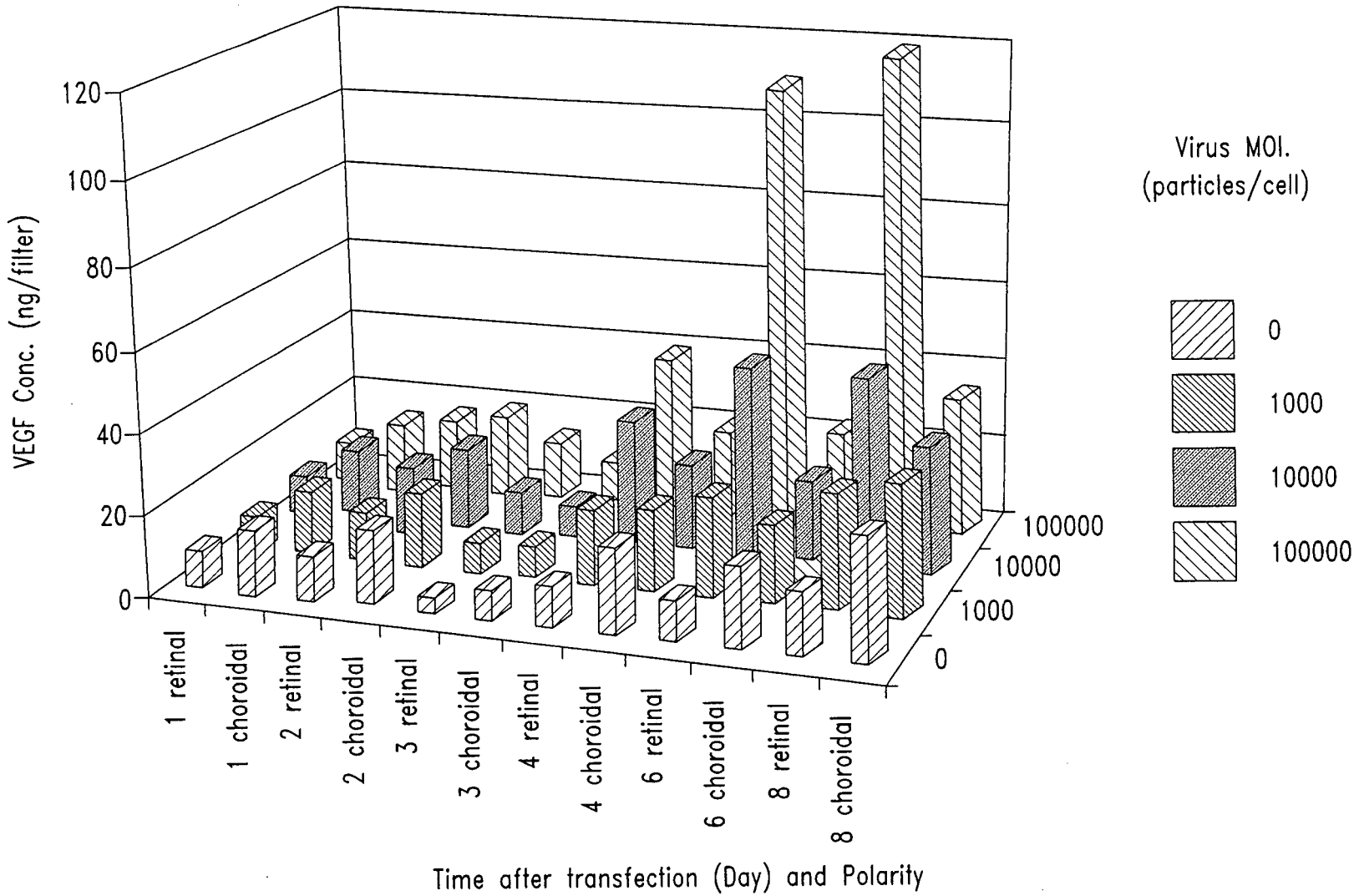

Fig. 24

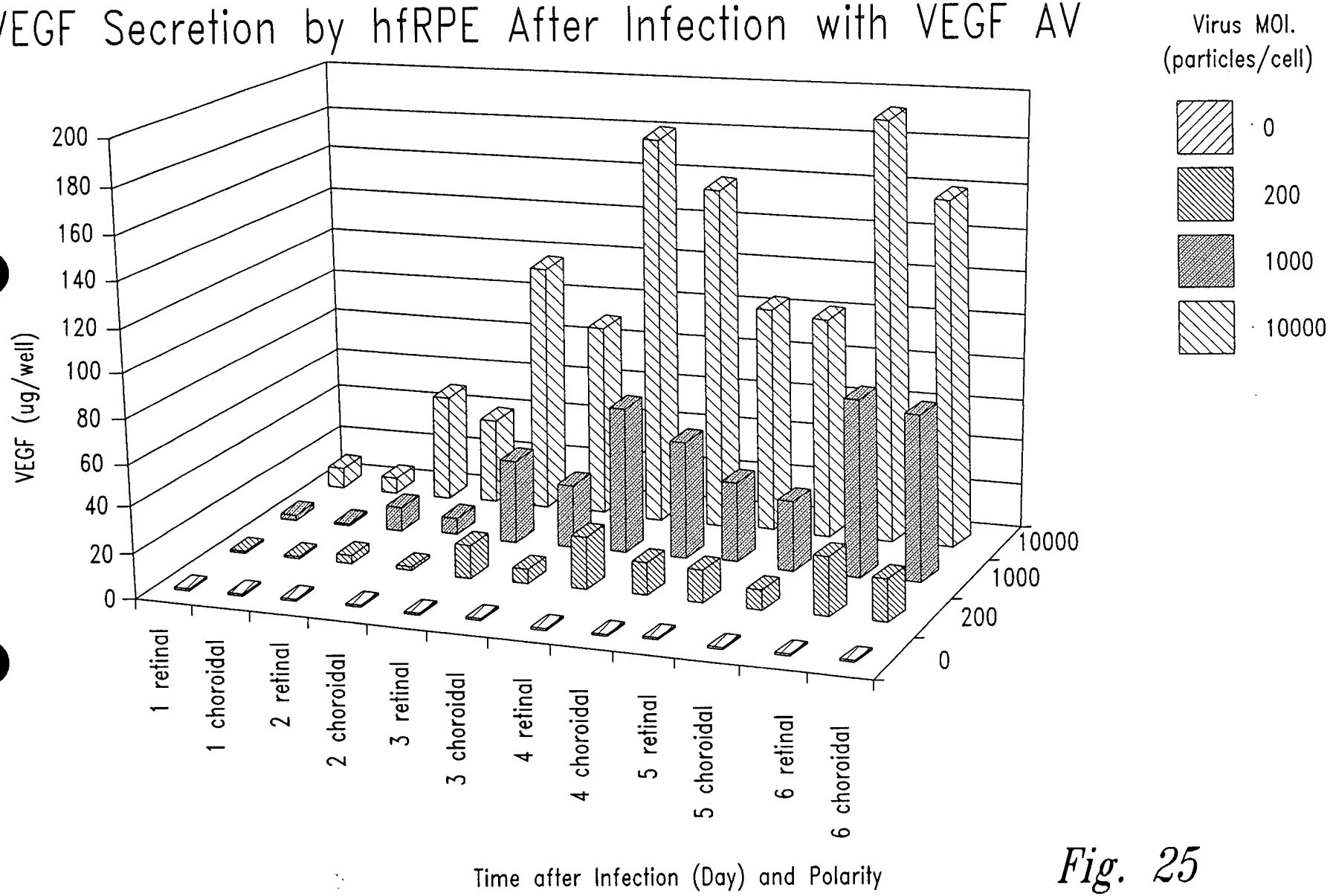

Fig. 25

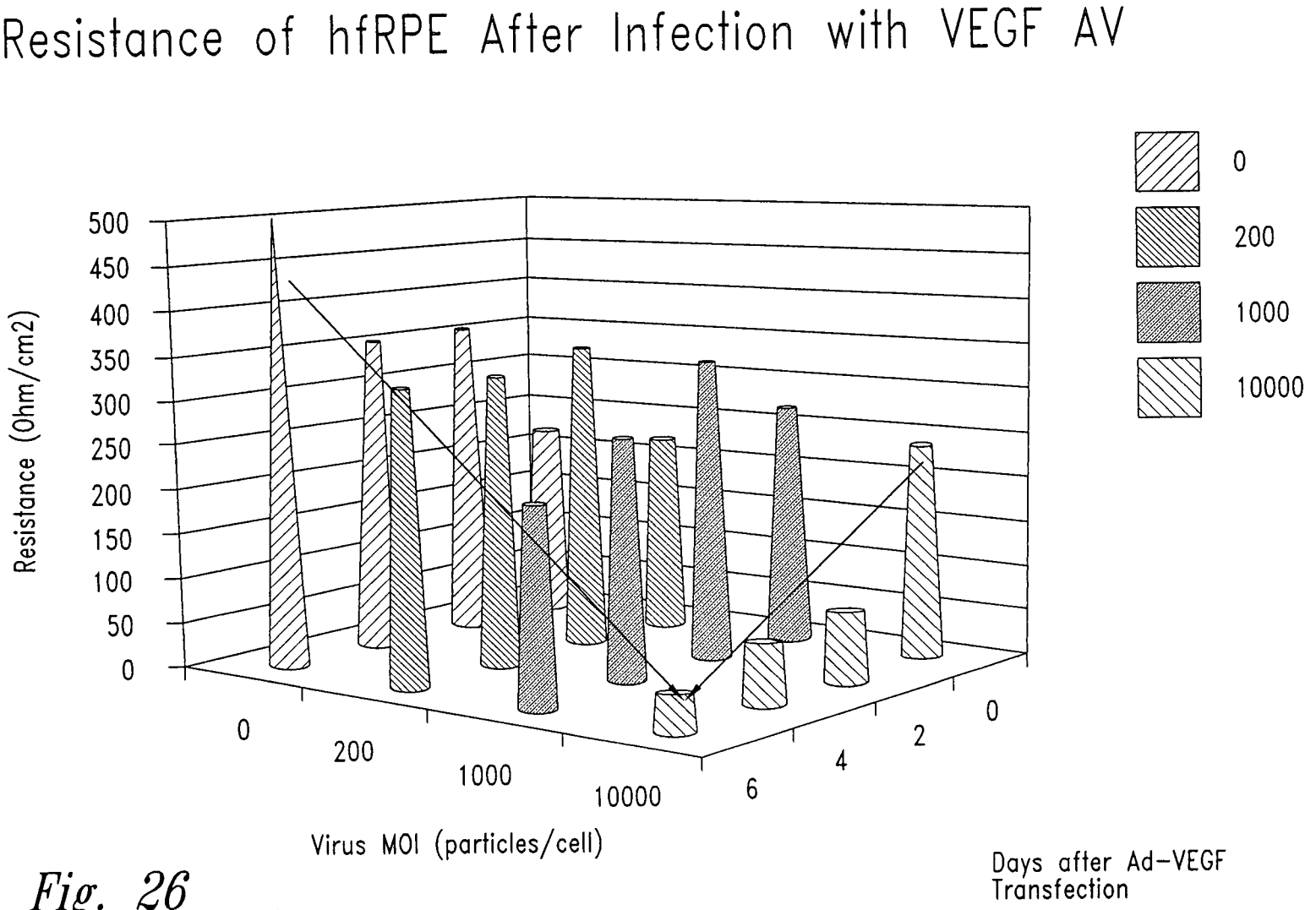
Resistance of hfRPE After Infection with VEGF AV
Resistance (Ohm/cm2)
500
450
400
350
300
250
200
150
100
50
0
0
200
1000
10000
Virus MOI (particles/cell)
0
2
4
6
Days after Ad-VEGF Transfection
0
200
1000
10000

Fig. 26

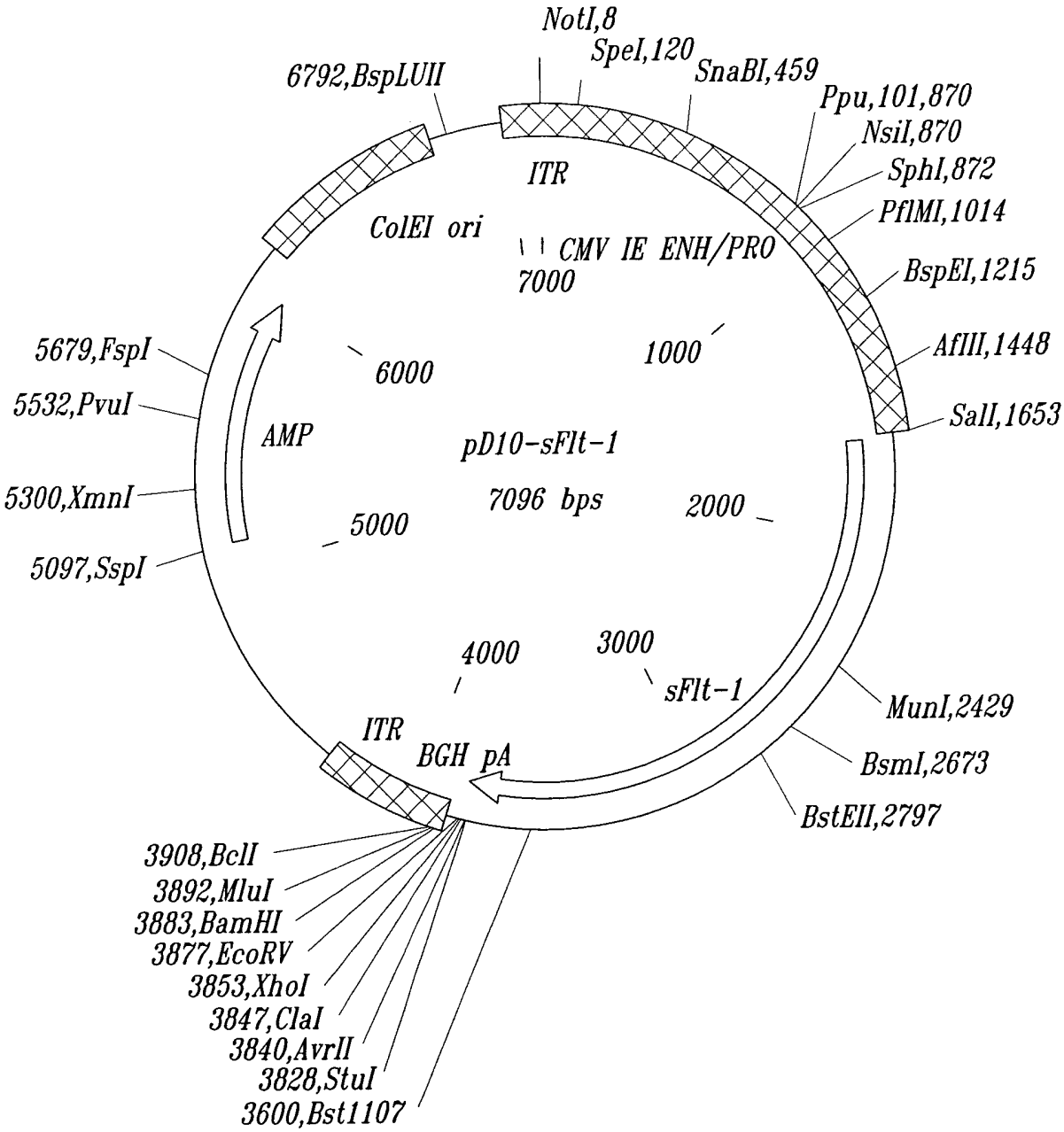
NotI,8
SpeI,120
SnaBI,459
Ppu,101,870
NsiI,870
SphI,872
PflMI,1014
BspEI,1215
AflII,1448
SalI,1653
MunI,2429
BsmI,2673
BstEII,2797
3908,BclI
3892,MluI
3883,BamHI
3877,EcoRV
3853,XhoI
3847,ClaI
3840,AvrII
3828,StuI
3600,Bst1107
5097,SspI
5300,XmnI
5532,PvuI
5679,FspI
6792,BspLUII
ITR
ColEI ori
CMV IE ENH/PRO
7000
1000
2000
3000
4000
5000
6000
AMP
pD10-sFlt-1
7096 bps
sFlt-1
ITR
BGH pA

Fig. 27

Nucleotide Sequence of pD10-SFlt-1

AAAACTTGCGGCCGCGGAATTTCGACTCTAGGCCATTGCATACGTTGTATCTATATCATAATATGTACATTTATATTGGCTCATGTCCAATATGACCGC
CATGTTGACATTGATTATTGACTAGTTATTAATAGTAATCAATTACGGGGTCATTAGTTCATAGCCCATATATGGAGTTCCGCGTTACATAACTTACGG
TAAATGGCCCGCCTGGCTGACCGCCCAACGACCCCCGCCCATTGACGTCAATAATGACGTATGTTCCCATAGTAACGCCAATAGGGACTTTCCATTGAC
GTCAATGGGTGGAGTATTTACGGTAAACTGCCCACTTGGCAGTACATCAAGTGTATCATATGCCAAGTCCGCCCCCTATTGACGTCAATGACGGTAAAT
GGCCCGCCTGGCATTATGCCCAGTACATGACCTTACGGGACTTTCCTACTTGGCAGTACATCTACGTATTAGTCATCGCTATTACCATGGTGATGCGGT
TTTGGCAGTACACCAATGGGCGTGGATAGCGGTTTGACTCACGGGGATTTCCAAGTCTCCACCCCATTGACGTCAATGGGAGTTTGTTTTGGCACCAAA
ATCAACGGGACTTTCCAAAATGTCGTAATAACCCCGCCCCGTTGACGCAAATGGGCGGTAGGCGTGTACGGTGGGAGGTCTATATAAGCAGAGCTCGTT
TAGTGAACCGTCAGATCGCCTGGAGACGCCATCCACGCTGTTTTGACCTCCATAGAAGACACCGGGACCGATCCAGCCTCCGCGGCCGGGAACGGTGCA
TTGGAACGCGGATTCCCCGTGCCAAGAGTGACGTAAGTACCGCCTATAGACTCTATAGGCACACCCCTTTGGCTCTTATGCATGCTATACTGTTTTTGG
CTTGGGGCCTATACACCCCCGCTCCTTATGCTATAGGTGATGGTATAGCTTAGCCTATAGGTGTGGGTTATTGACCATTATTGACCACTCCCCTATTGG
TGACGATACTTTCCATTACTAATCCATAACATGGCTCTTTGCCACAACTATCTCTATTGGCTATATGCCAATACTCTGTCCTTCAGAGACTGACACGGA
CTCTGTATTTTTACAGGATGGGGTCCATTTATTATTTACAAATTCACATATACAACAACGCCGTCCCCCGTGCCCGCAGTTTTTATTAAACATAGCGTG
GGATCTCCGACATCTCGGGTACGTGTTCCGGACATGGGCTCTTCTCCGGTAGCGGCGGAGCTTCCACATCCGAGCCCTGGTCCCATCCGTCCAGCGGCT
CATGGTCGCTCGGCAGCTCCTTGCTCCTAACAGTGGAGGCCAGACTTAGGCACAGCACAATGCCCACCACCACCAGTGTGCCGCACAAGGCCGTGGCGG
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TGTTGTATTCTGATAAGAGTCAGAGGTAACTCCCGTTGCGGTGCTGTTAACGGTGGAGGGCAGTGTAGTCTGAGCAGTACTCGTTGCTGCCGCGCGCGC
CACCAGACATAATAGCTGACAGACTAACAGACTGTTCCTTTCCATGGGTCTTTTCTGCAGTCACCGTCGTCGACCTAAGAATTCGCCCTTTCACCATGG
TCAGCTACTGGGACACCGGGGTCCTGCTGTGCGCGCTGCTCAGCTGTCTGCTTCTCACAGGATCTAGTTCAGGTTCAAAATTAAAAGATCCTGAACTGA
GTTTAAAAGGCACCCAGCACATCATGCAAGCAGGCCAGACACTGCATCTCCAATGCAGGGGGGAAGCAGCCCATAAATGGTCTTTGCCTGAAATGGTGA
GTAAGGAAAGCGAAAGGCTGAGCATAACTAAATCTGCCTGTGGAAGAAATGGCAAACAATTCTGCAGTACTTTAACCTTGAACACAGCTCAAGCAAACC
ACACTGGCTTCTACAGCTGCAAATATCTAGCTGTACCTACTTCAAAGAAGAAGGAAACAGAATCTGCAATCTATATATTTATTAGTGATACAGGTAGAC
CTTTCGTAGAGATGTACAGTGAAATCCCCGAAATTATACACATGACTGAAGGAAGGGAGCTCGTCATTCCCTGCCGGGTTACGTCACCTAACATCACTG
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GGAGTTACCCTGATGAAAAAAATAAGAGAGCTTCCGTAAGGCGACGAATTGACCAAAGCAATTCCCATGCCAACATATTCTACAGTGTTCTTACTATTG
ACAAAATGCAGAACAAAGACAAAGGACTTTATACTTGTCGTGTAAGGAGTGGACCATCATTCAAATCTGTTAACACCTCAGTGCATATATATGATAAAG
CATTCATCACTGTGAAACATCGAAAACAGCAGGTGCTTGAAACCGTAGCTGGCAAGCGGTCTTACCGGCTCTCTATGAAAGTGAAGGCATTTCCCTCGC
CGGAAGTTGTATGGTTAAAAGATGGGTTACCTGCGACTGAGAAATCTGCTCGCTATTTGACTCGTGGCTACTCGTTAATTATCAAGGACGTAACTGAAG
AGGATGCAGGGAATTATACAATCTTGCTGAGCATAAAACAGTCAAATGTGTTTAAAAACCTCACTGCCACTCTAATTGTCAATGTGAAACCCCAGATTT
ACGAAAAGGCCGTGTCATCGTTTCCAGACCCGGCTCTCTACCCACTGGGCAGCAGACAAATCCTGACTTGTACCGCATATGGTATCCCTCAACCTACAA
TCAAGTGGTTCTGGCACCCCTGTAACCATAATCATTCCGAAGCAAGGTGTGACTTTTGTTCCAATAATGAAGAGTCCTTTATCCTGGATGCTGACAGCA
ACATGGGAAACAGAATTGAGAGCATCACTCAGCGCATGGCAATAATAGAAGGAAAGAATAAGATGGCTAGCACCTTGGTTGTGGCTGACTCTAGAATTT
CTGGAATCTACATTTGCATAGCTTCCAATAAAGTTGGGACTGTGGGAAGAAACATAAGCTTTTATATCACAGATGTGCCAAATGGGTTTCATGTTAACT
TGGAAAAAATGCCGACGGAAGGAGAGGACCTGAAACTGTCTTGCACAGTTAACAAGTTCTTATACAGAGACGTTACTTGGATTTTACTGCGGACAGTTA
ATAACAGAACAATGCACTACAGTATTAGCAAGCAAAAAATGGCCATCACTAAGGAGCACTCCATCACTCTTAATCTTACCATCATGAATGTTTCCCTGC
AAGATTCAGGCACCTATGCCTGCAGAGCCAGGAATGTATACACAGGGGAAGAAATCCTCCAGAAGAAAGAAATTACAATCAGAGGTGAGCACTGCAACA
AAAAGGCTGTTTTCTCTCGGATCTCCAAATTTAAAAGCACAAGGAATGATTGTACCACACAAAGTAATGTAAAACATTAAAGGACTCATTAAAAAGTAA
CAGTTGTCTCATATCATCTTGATTTATTGTCACTGTTGCTAACTTTCAGGCTCAAGGGCGAATTCAGGCCTAAGCTTCCTAGGTATCGATCTCGAGCAA
GTCTAGAAAGCCATGGATATCGGATCCACTACGCGTTAGAGCTCGCTGATCAGCCTCGACTGTGCCTTCTAGTTGCCAGCCATCTGTTGTTTGCCCCTC

Fig. 28A

CCCCGTGCCTTCCTTGACCCTGGAAGGTGCCACTCCCACTGTCCTTTCCTAATAAAATGAGGAAATTGCATCGCATTGTCTGAGTAGGTGTCATTCTAT
TCTGGGGGGTGGGGTGGGGCAGGACAGCAAGGGGGAGGATTGGGAAGACAATAGCAGGGGGGTGGGCGAAGAACTCCAGCATGAGATCCCCGCGCTGGA
GGATCATCCAGCTAGCAAGTCCCATCAGTGATGGAGTTGGCCACTCCCTCTCTGCGCGCTCGCTCGCTCACTGAGGCCGGGCGACCAAAGGTCGCCCGA
CGCCCGGGCTTTGCCCGGGCGGCCTCAGTGAGCGAGCGAGCGCGCCAGCGATTCTCTTGTTTGCTCCAGACTCTCAGGCAATGACCTGATAGCCTTTGT
AGAGACCTCTCAAAAATAGCTACCCTCTCCGGCATGAATTTATCAGCTAGAACGGTTGAATATCATATTGATGGTGATTTGACTGTCTCCGGCCTTTCT
CACCCGTTTGAATCTTTACCTACACATTACTCAGGCATTGCATTTAAAATATATGAGGGTTCTAAAAATTTTTATCCTTGCGTTGAAATAAAGGCTTCT
CCCGCAAAAGTATTACAGGGTCATAATGTTTTTGGTACAACCGATTTAGCTTTATGCTCTGAGGCTTTATTGCTTAATTTTGCTAATTCTTTGCCTTGC
CTGTATGATTTATTGGATGTTGGAATTCCTGATGCGGTATTTTCTCCTTACGCATCTGTGCGGTATTTCACACCGCATATGGTGCACTCTCAGTACAAT
CTGCTCTGATGCCGCATAGTTAAGCCAGCCCCGACACCCGCCAACACCCGCTGACGCGCCCTGACGGGCTTGTCTGCTCCCGGCATCCGCTTACAGACA
AGCTGTGACCGTCTCCGGGAGCTGCATGTGTCAGAGGTTTTCACCGTCATCACCGAAACGCGCGAGACGAAAGGGCCTCGTGATACGCCTATTTTTATA
GGTTAATGTCATGATAATAATGGTTTCTTAGACGTCAGGTGGCACTTTTCGGGGAAATGTGCGCGGAACCCCTATTTGTTTATTTTTCTAAATACATTC
AAATATGTATCCGCTCATGAGACAATAACCCTGATAAATGCTTCAATAATATTGAAAAAGGAAGAGTATGAGTATTCAACATTTCCGTGTCGCCCTTAT
TCCCTTTTTTGCGGCATTTTGCCTTCCTGTTTTTGCTCACCCAGAAACGCTGGTGAAAGTAAAAGATGCTGAAGATCAGTTGGGTGCACGAGTGGGTTA
CATCGAACTGGATCTCAACAGCGGTAAGATCCTTGAGAGTTTTCGCCCCGAAGAACGTTTTCCAATGATGAGCACTTTTAAAGTTCTGCTATGTGGCGC
GGTATTATCCCGTATTGACGCCGGGCAAGAGCAACTCGGTCGCCGCATACACTATTCTCAGAATGACTTGGTTGAGTACTCACCAGTCACAGAAAAGCA
TCTTACGGATGGCATGACAGTAAGAGAATTATGCAGTGCTGCCATAACCATGAGTGATAACACTGCGGCCAACTTACTTCTGACAACGATCGGAGGACC
GAAGGAGCTAACCGCTTTTTTGCACAACATGGGGGATCATGTAACTCGCCTTGATCGTTGGGAACCGGAGCTGAATGAAGCCATACCAAACGACGAGCG
TGACACCACGATGCCTGTAGCAATGGCAACAACGTTGCGCAAACTATTAACTGGCGAACTACTTACTCTAGCTTCCCGGCAACAATTAATAGACTGGAT
GGAGGCGGATAAAGTTGCAGGACCACTTCTGCGCTCGGCCCTTCCGGCTGGCTGGTTTATTGCTGATAAATCTGGAGCCGGTGAGCGTGGGTCTCGCGG
TATCATTGCAGCACTGGGGCCAGATGGTAAGCCCTCCCGTATCGTAGTTATCTACACGACGGGGAGTCAGGCAACTATGGATGAACGAAATAGACAGAT
CGCTGAGATAGGTGCCTCACTGATTAAGCATTGGTAACTGTCAGACCAAGTTTACTCATATATACTTTAGATTGATTTAAAACTTCATTTTTAATTTAA
AAGGATCTAGGTGAAGATCCTTTTTGATAATCTCATGACCAAAATCCCTTAACGTGAGTTTTCGTTCCACTGAGCGTCAGACCCCGTAGAAAAGATCAA
AGGATCTTCTTGAGATCCTTTTTTTCTGCGCGTAATCTGCTGCTTGCAAACAAAAAAACCACCGCTACCAGCGGTGGTTTGTTTGCCGGATCAAGAGCT
ACCAACTCTTTTTCCGAAGGTAACTGGCTTCAGCAGAGCGCAGATACCAAATACTGTCCTTCTAGTGTAGCCGTAGTTAGGCCACCACTTCAAGAACTC
TGTAGCACCGCCTACATACCTCGCTCTGCTAATCCTGTTACCAGTGGCTGCTGCCAGTGGCGATAAGTCGTGTCTTACCGGGTTGGACTCAAGACGATA
GTTACCGGATAAGGCGCAGCGGTCGGGCTGAACGGGGGGTTCGTGCACACAGCCCAGCTTGGAGCGAACGACCTACACCGAACTGAGATACCTACAGCG
TGAGCTATGAGAAAGCGCCACGCTTCCCGAAGGGAGAAAGGCGGACAGGTATCCGGTAAGCGGCAGGGTCGGAACAGGAGAGCGCACGAGGGAGCTTCC
AGGGGGAAACGCCTGGTATCTTTATAGTCCTGTCGGGTTTCGCCACCTCTGACTTGAGCGTCGATTTTTGTGATGCTCGTCAGGGGGGCGGAGCCTATG
GAAAAACGCCAGCAACGCGGCCTTTTTACGGTTCCTGGCCTTTTGCTGGCCTTTTGCTCACATGTTCTTTCCTGCGTTATCCCCTGATTCTGTGGATAA
CCGTATTACCGCCTTTGAGTGAGCTGATACCGCTCGCCGCAGCCGAACGACCGAGCGCAGCGAGTCAGTGAGCGAGGAAGCGGAAGAGCGCCCAATACG
CAAACCGCCTCTCCCCGCGCGTTGGCCGATTCATTAATGCAGCTGGCGCGCTCGCTCGCTCACTGAGGCCGCCCGGGCAAAGCCCGGGCGTCGGGCGAC
CTTTGGTCGCCCGGCCTCAGTGAGCGAGCGAGCGCGCAGAGAGGGAGTGGCCAACTCCATCACTGAT

Fig. 28B

HumanFGF-20

atggctcccttagccgaagtcgggggctttctgggcggcctggagggcttgggccagcag
M A P L A E V G G F L G G L E G L G Q Q

gtgggttcgcatttcctgttgcctcctgccggggagcggccgccgctgctgggcgagcgc
V G S H F L L P P A G E R P P L L G E R

aggagcgcggcggagcggagcgcgcgcggcgggccgggggctgcgcagctggcgcacctg
R S A A E R S A R G G P G A A Q L A H L

cacggcatcctgcgccgccggcagctctattgccgcaccggcttccacctgcagatcctg
H G I L R R R Q L Y C R T G F H L Q I L

cccgacggcagcgtgcagggcacccggcaggaccacagcctcttcggtatcttggaattc
P D G S V Q G T R Q D H S L F G I L E F

atcagtgtggcagtgggactggtcagtattagaggtgtggacagtggtctctatcttgga
I S V A V G L V S I R G V D S G L Y L G

atgaatgacaaaggagaactctatggatcagagaaacttacttccgaatgcatctttagg
M N D K G E L Y G S E K L T S E C I F R

gagcagtttgaagagaactggtataacacctattcatctaacatatataaacatggagac
E Q F E E N W Y N T Y S S N I Y K H G D

actggccgcaggtattttgtggcacttaacaaagacggaactccaagagatggcgccagg
T G R R Y F V A L N K D G T P R D G A R

tccaagaggcatcagaaatttacacatttcttacctagaccagtggatccagaaagagtt
S K R H Q K F T H F L P R P V D P E R V

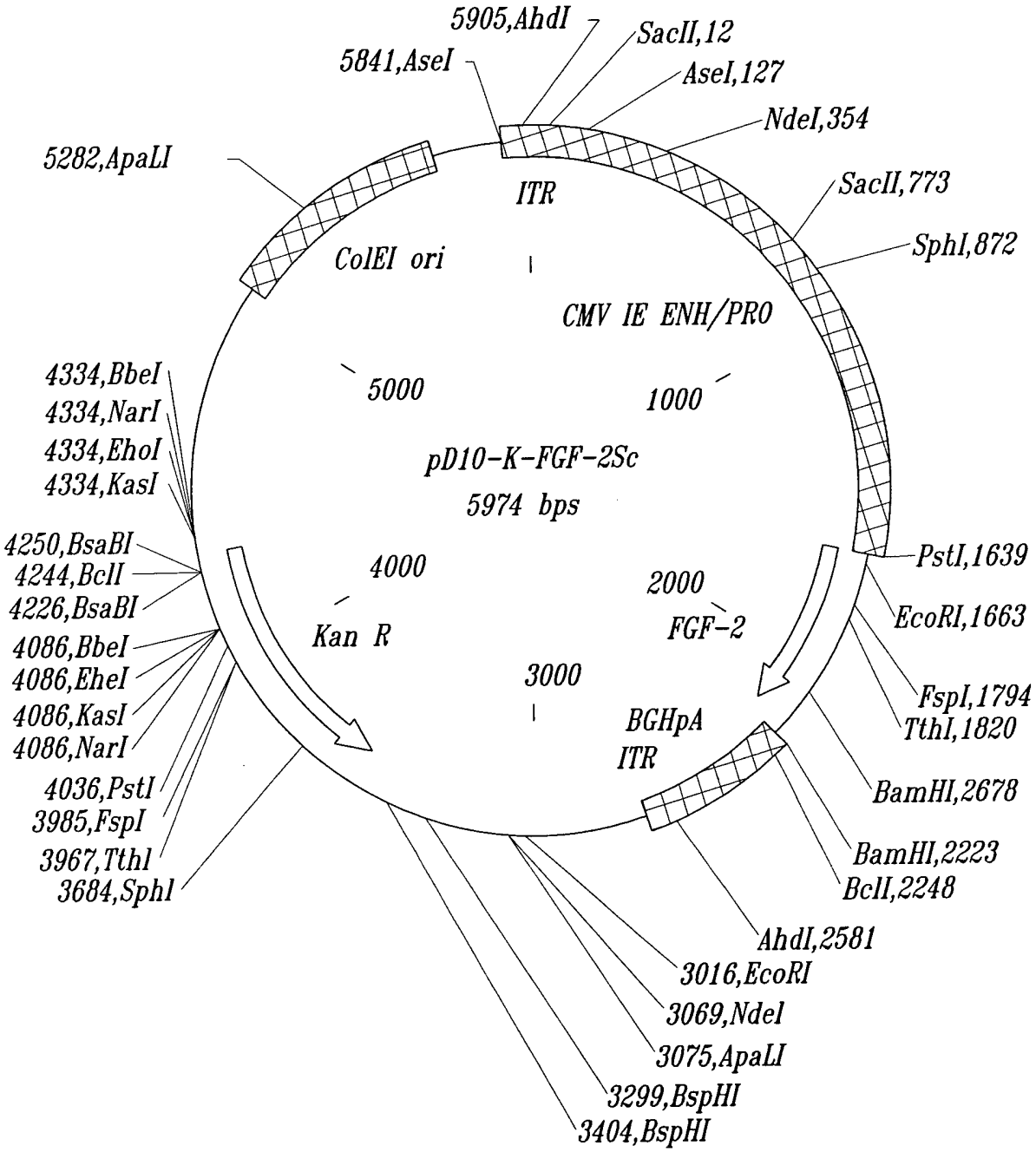
ccagaattgtacaaggacctactgatgtacacttga
P E L Y K D L L M Y T

Fig. 29

Mouse FGF-21 cDNA in pGEM-T

```
gagcgcagccctgatggaatggatgagatctagagttgggaccctgggactgtgggtccg   SEQ ID NO: 1
          M  E  W  M  R  S  R  V  G  T  L  G  L  W  V  R        SEQ ID NO: 2

actgctgctggctgtcttcctgctgggggtctaccaagcatacccccatccctgactccag
 L  L  L  A  V  F  L  L  G  V  Y  Q  A  Y  P  I  P  D  S  S

ccccctcctccagtttgggggtcaagtccggcagaggtacctctacacagatgacgacca
 P  L  L  Q  F  G  G  Q  V  R  Q  R  Y  L  Y  T  D  D  D  Q

agacactgaagcccacctggagatcagggaggatggaacagtggtaggcgcagcacaccg
 D  T  E  A  H  L  E  I  R  E  D  G  T  V  V  G  A  A  H  R

cagtccagaaagtctcctggagctcaaagccttgaagccaggggtcattcaaatcctggg
 S  P  E  S  L  L  E  L  K  A  L  K  P  G  V  I  Q  I  L  G

tgtcaaagcctctaggtttctttgccaacagccagatggagctctctatggatcgcctca
 V  K  A  S  R  F  L  C  Q  Q  P  D  G  A  L  Y  G  S  P  H

ctttgatcctgaggcctgcagcttcagagaactgctgctggaggacggttacaatgtgta
 F  D  P  E  A  C  S  F  R  E  L  L  L  E  D  G  Y  N  V  Y

ccagtctgaagcccatggcctgcccctgcgtctgcctcagaaggactccccaaaccagga
 Q  S  E  A  H  G  L  P  L  R  L  P  Q  K  D  S  P  N  Q  D

tgcaacatcctggggacctgtgcgcttcctgcccatgccaggcctgctccacgagcccca
 A  T  S  W  G  P  V  R  F  L  P  M  P  G  L  L  H  E  P  Q

agaccaagcaggattcctgcccccagagcccccagatgtgggctcctctgacccccctgag
 D  Q  A  G  F  L  P  P  E  P  P  D  V  G  S  S  D  P  L  S

catggtagagcctttacagggccgaagccccagctatgcgtcctgactcttcctgaatc
 M  V  E  P  L  Q  G  R  S  P  S  Y  A  S
```

Fig. 30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SacII,12
5841,AseI
AseI,127
NdeI,354
5282,ApaLI
ITR
SacII,773
SphI,872
ColEI ori
CMV IE ENH/PRO
4334,BbeI
4334,NarI
4334,EhoI
4334,KasI
5000
1000
pD10-K-FGF-2Sc
5974 bps
4250,BsaBI
4244,BclI
4226,BsaBI
4000
2000
PstI,1639
EcoRI,1663
FGF-2
Kan R
4086,BbeI
4086,EheI
4086,KasI
4086,NarI
3000
FspI,1794
TthI,1820
BGHpA
ITR
4036,PstI
3985,FspI
3967,TthI
3684,SphI
BamHI,2678
BamHI,2223
BclII,2248
AhdI,2581
3016,EcoRI
3069,NdeI
3075,ApaLI
3299,BspHI
3404,BspHI

Fig. 31

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AGGGTCATAATGTTTTTGGTACAACCGATTTAGCTTTATGCTCTGAGGCTTTATTGCTTAATTTTGCTAATTCTTTGCCTTGCCTGTATGATTTATT
GGATGTTGGAATTCCTGATGCGGTATTTTCTCCTTACGCATCTGTGCGGTATTTCACACCGCATATGGTGCACTCTCAGTACAATC

Fig. 32A

TGCTCTGATGCCGCATAGTTAAGCCAGCCCCGACACCCGCCAACACCCGCTGACGCGCCCTGACGGGCTTGTCTGCTCCCGGCATCCGCTTACAGAC
AAGCTGTGACCGTCTCCGGGAGCTGCATGTGTCAGAGGTTTTCACCGTCATCACCGAAACGCGCGAGACGAAAGGGCCTCGTGATACGCCTATTTTT
ATAGGTTAATGTCATGATAATAATGGTTTCTTAGACGTCAGGTGGCACTTTTCGGGGAAATGTGCGCGGAACCCCTATTTGTTTATTTTTCTAAATA
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GGGAGCGGCGATACCGTAAAGCACGAGGAAGCGGTCAGCCCATTCGCTTCAGCAATATCACGGGTAGCCAACGCTATGTCCTGATAGCGGTCCGCCA
CACCCAGCCGGCCACAGTCGATGAATCCAGAAAAGCGGCCATTTTCCACCATGATATTCGGCAAGCAGGCATCGCCATGGGTCACGACGAGATCCTC
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Fig. 32B

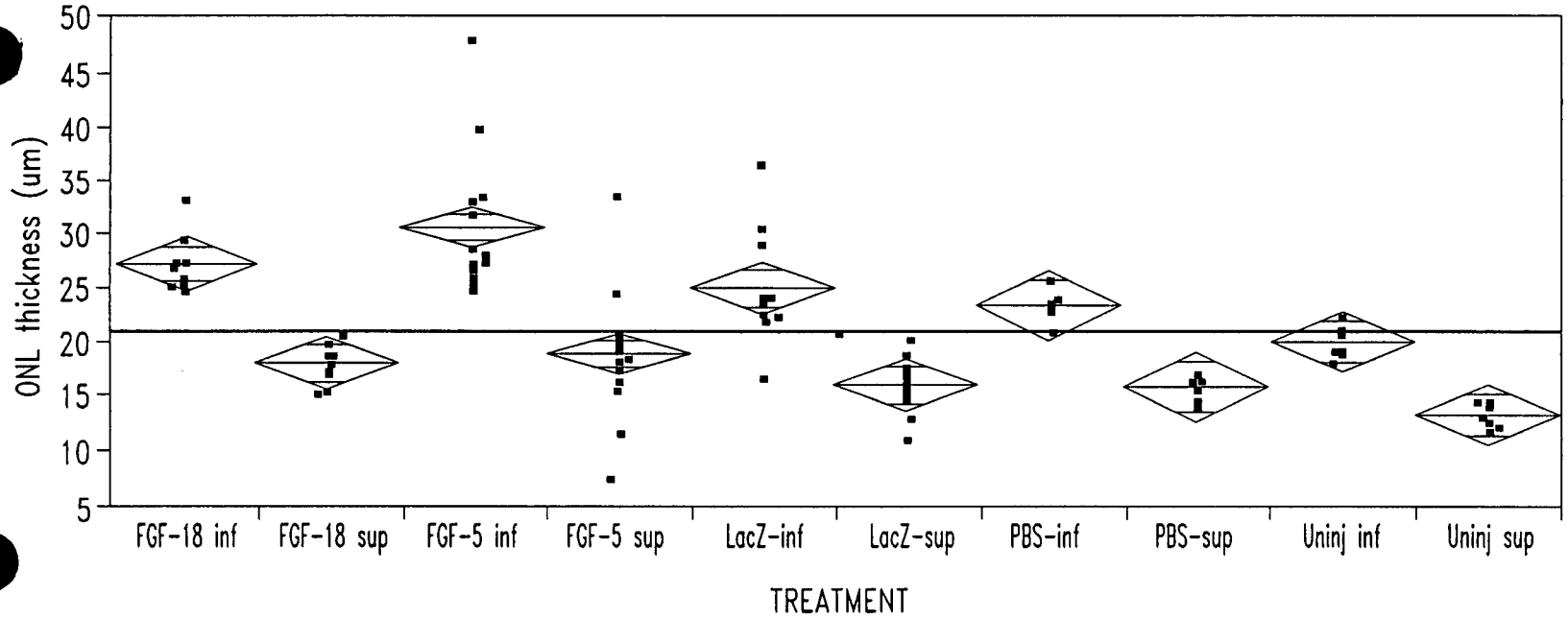

Fig. 33

Inhibition of HMVEC Proliferation by sFlt-1 rAAV

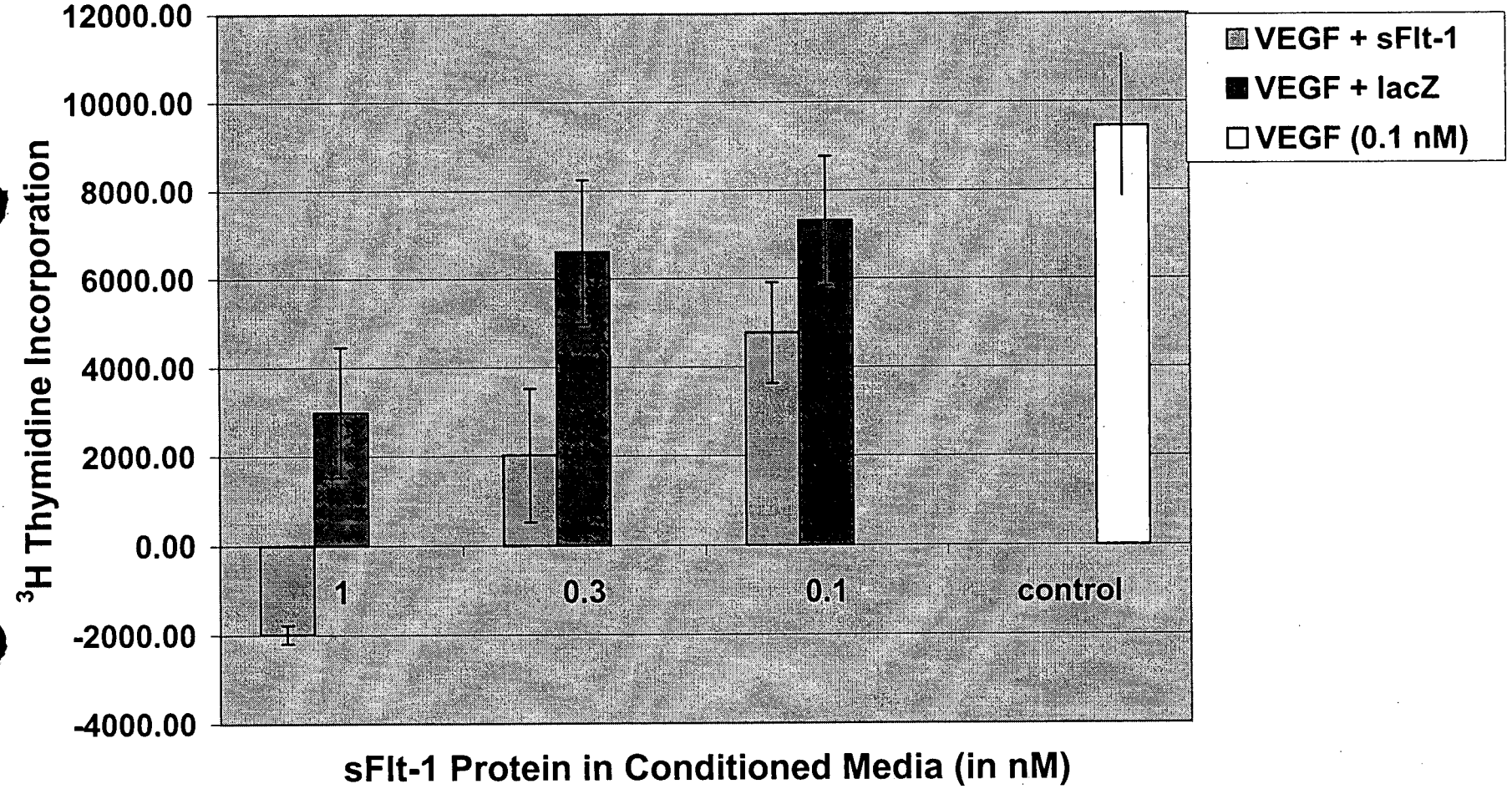

FIGURE 34

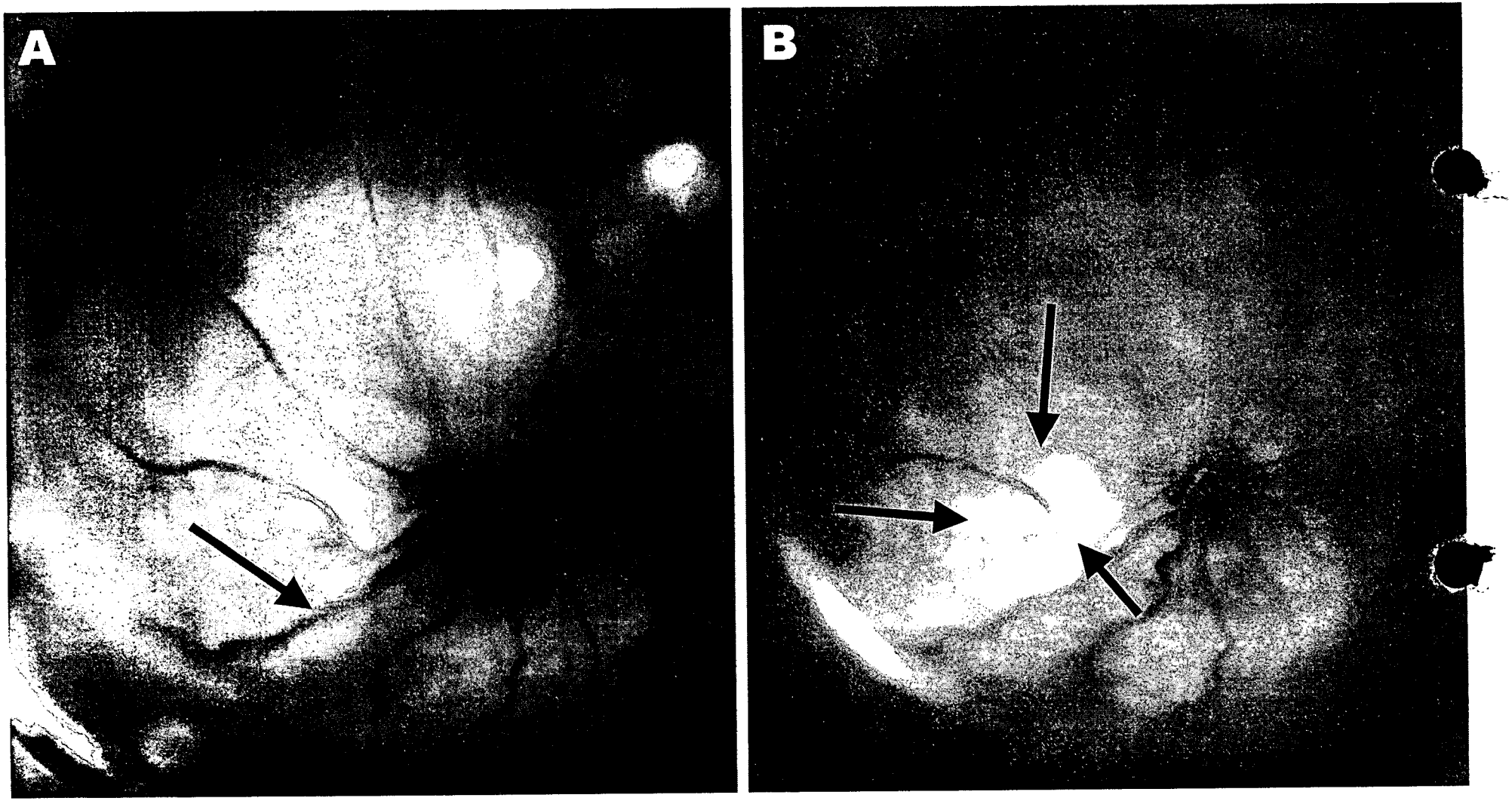

Figure 35. Fluorescein Angiography

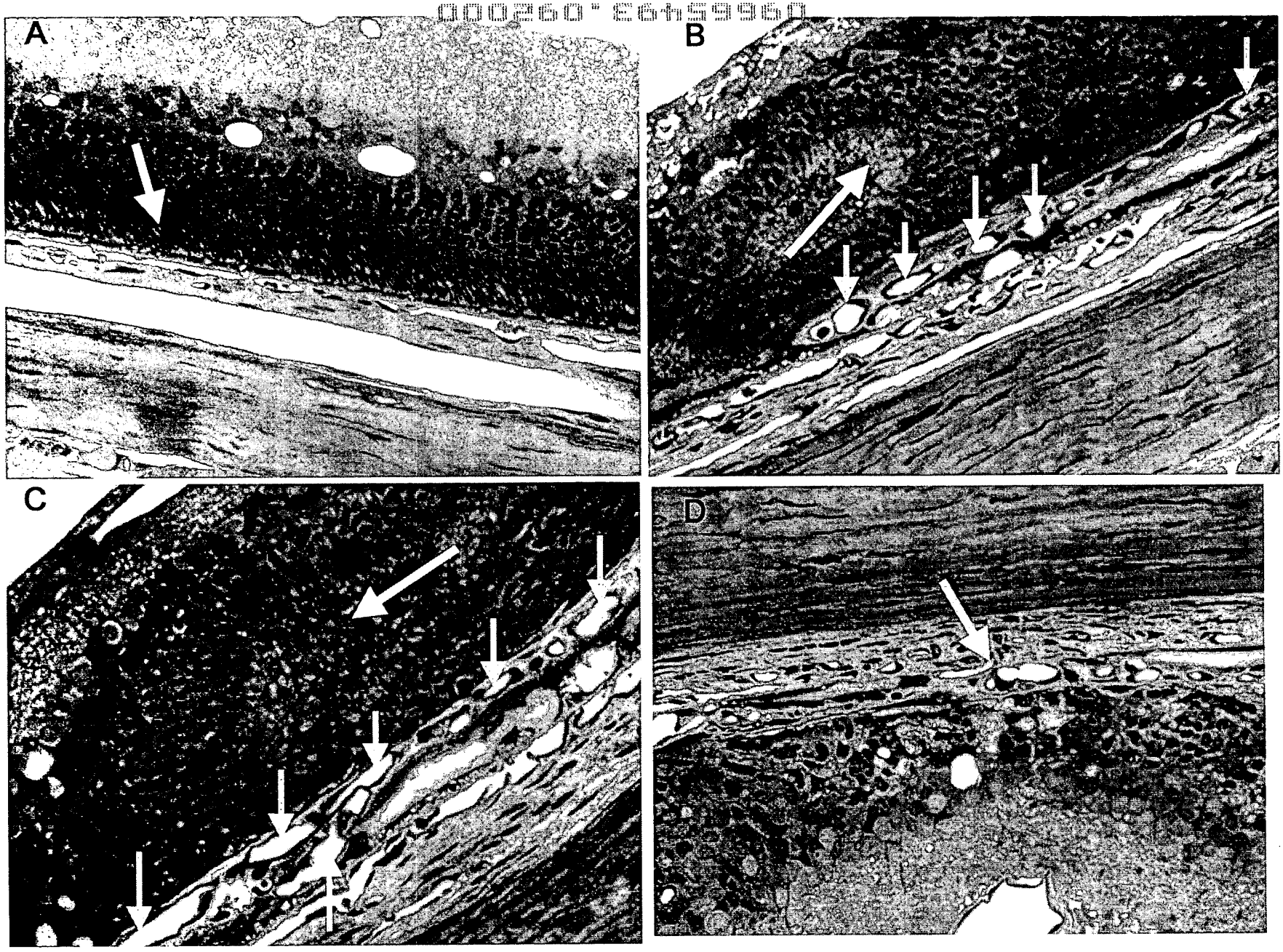

Figure 36. Epoxy Sections

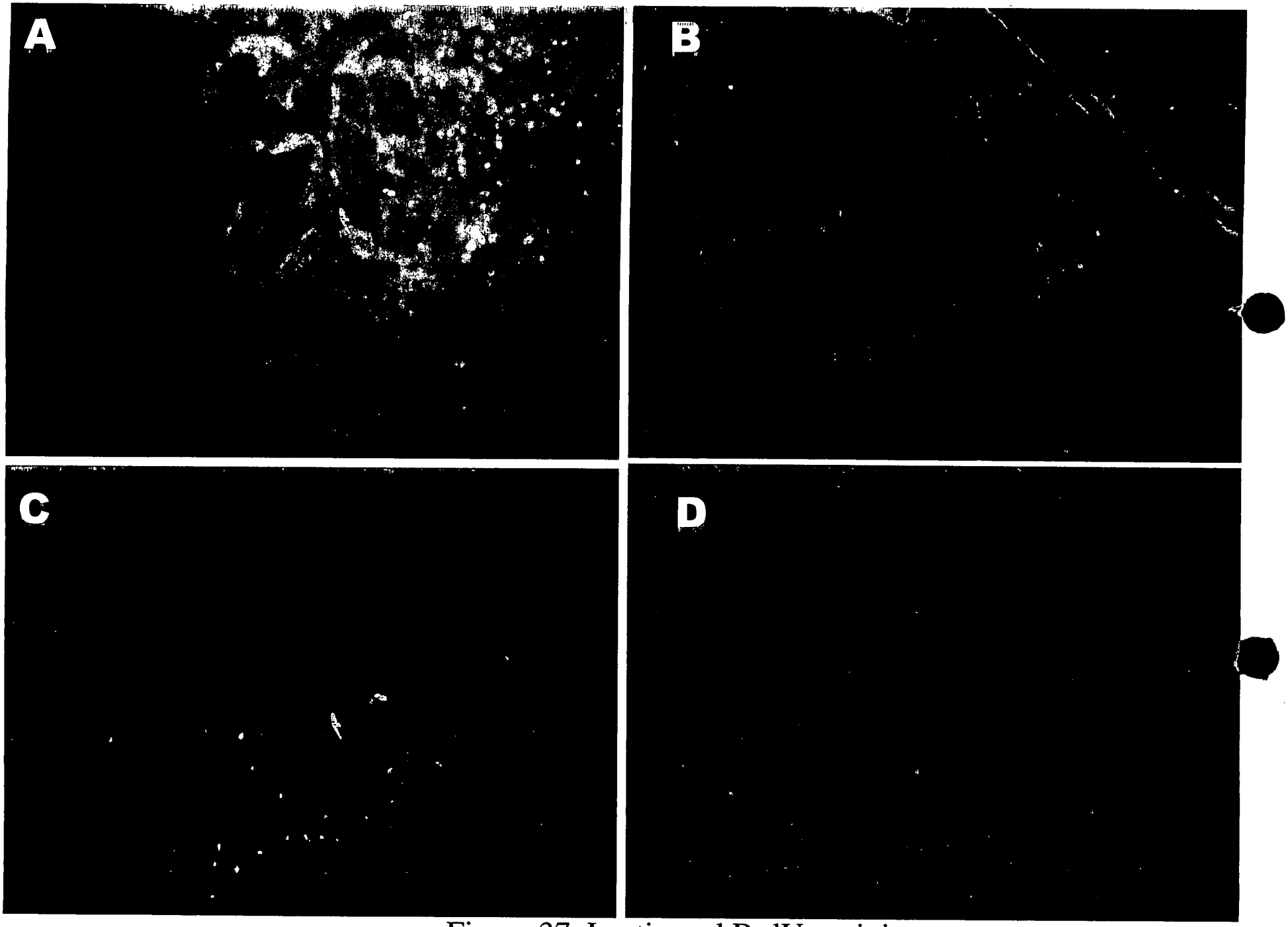

Figure 37. Lectin and BrdU staining

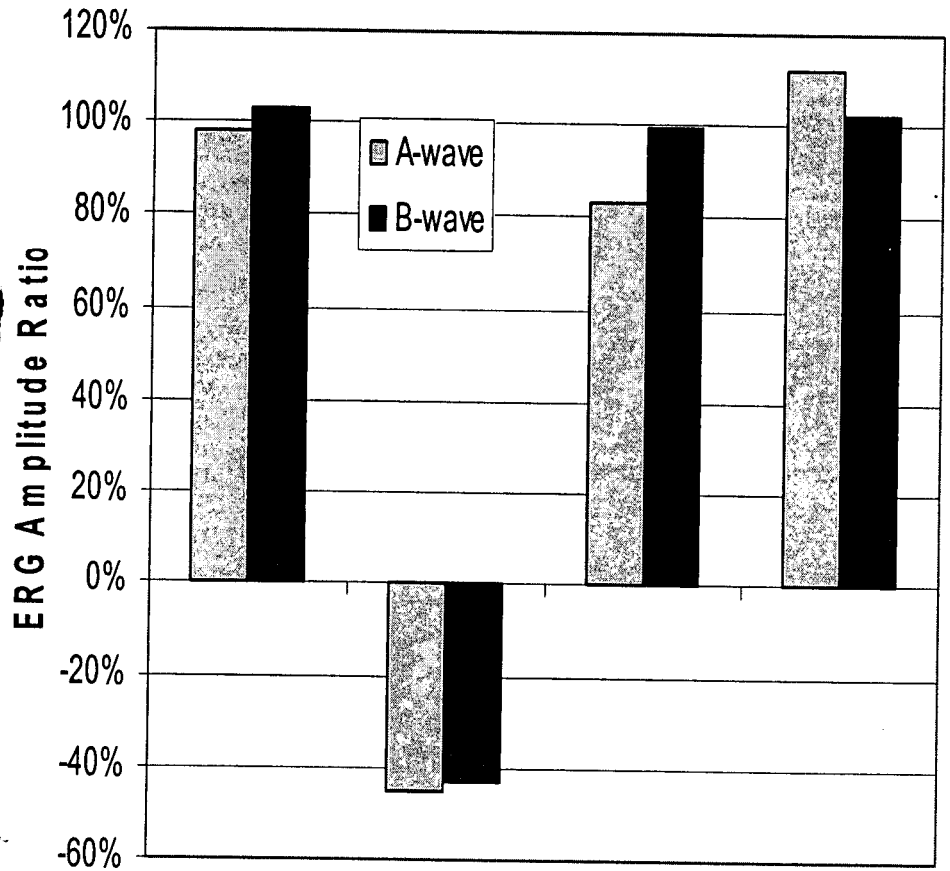

Figure 38A sFlt-1 rescue of ERGs

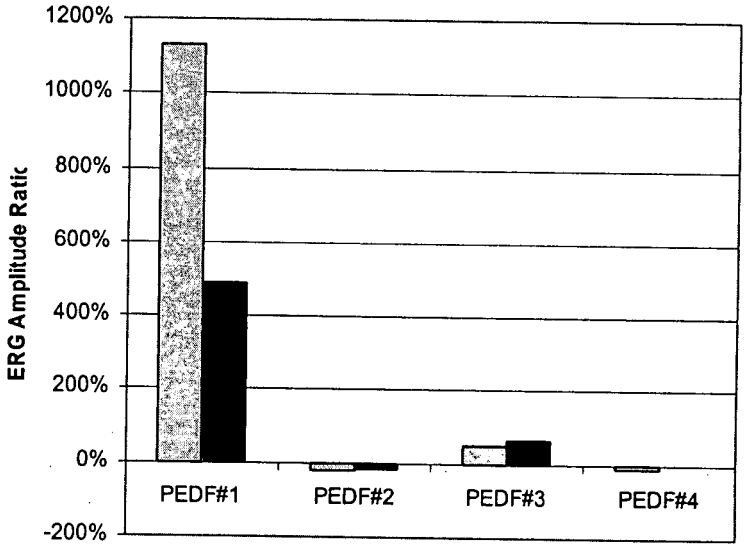

Figure38B. PEDF rescue of ERGs

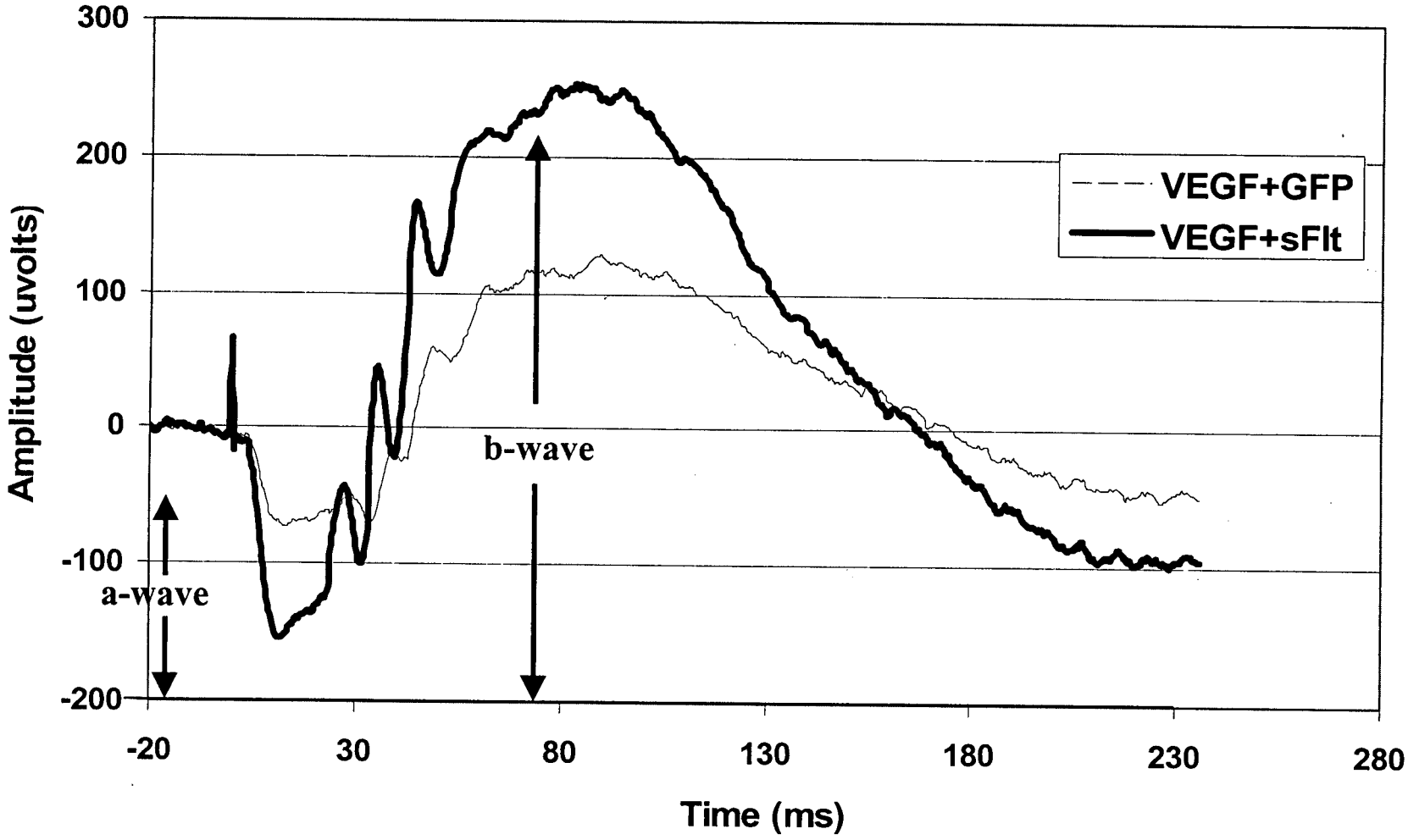

Figure 39. ERG of 070900 Rat#4 on 082300 (6 wk)